

VOL XXXI. NO. 6

APRIL 1 1938 38

MEDICAL LIBRARY

PROCEEDINGS  
*of the*  
ROYAL SOCIETY OF  
MEDICINE



LONGMANS, GREEN & C<sup>o</sup> LTD  
39, PATERNOSTER ROW, LONDON  
NEW YORK · BOMBAY · CALCUTTA · MADRAS

*All rights reserved.*

# 'POLLACCINE'

## for Hayfever

PATIENTS who are susceptible to hayfever during the summer months can be rendered relatively immune to attacks by a course of injection of pollen vaccine, given during the spring.

For those patients who have not yet commenced the prophylactic course, it will be necessary to give doses at comparatively short intervals in order to permit the attainment of a dose sufficiently large to confer adequate immunity.

'Pollaccine' is prepared in the Inoculation Department of St. Mary's Hospital, London (Founder, Sir A. E. Wright, M.D.), from the pollen of timothy grass (*Phleum pratense*). The toxins contained in the pollens of various grasses are so similar that 'Pollaccine' is the correct antigen for all true hayfever.

Further particulars concerning 'Pollaccine' and its prophylactic application will be sent on request.

**PARKE, DAVIS & CO.**  
**50 BEAK STREET, LONDON, W.1**

Laboratories : Hounslow, Middlesex. Inc. U.S.A., Liability Ltd.





## Clinical Section

President—B. T. PARSONS-SMITH, M.D.

[February 11, 1938]

### (?) Thyroid Cyst: Case for Diagnosis.—B. T. PARSONS-SMITH, M.D.

A. V., male, aged 70, has complained of sensations of discomfort in the upper part of the chest (region of right sternoclavicular joint) during the past six months; condition brought on by active movements of the right arm. Also complains of a hard swelling "at the top of the breast bone which interferes with movements of the head in certain directions by causing pressure on the collar".



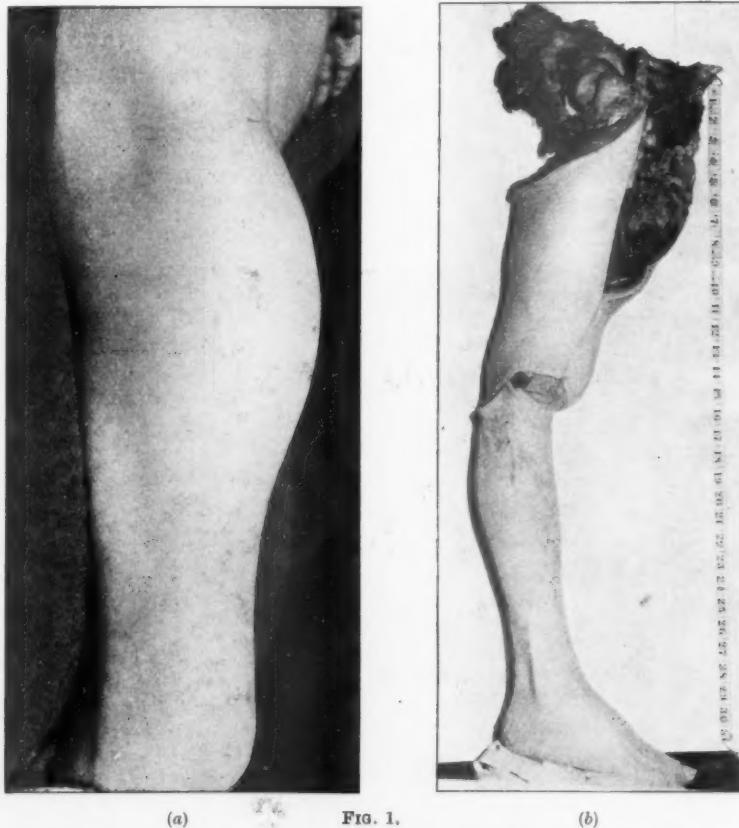
*Examination.*—Right sternoclavicular joint prominent; hard cystic swelling felt immediately above right sternoclavicular joint; moves with deglutition. Skiagrams show an oval cystic swelling, roughly the size of a small egg, in a clearly defined and smooth capsule.

Dr. EVAN BEDFORD said he thought the swelling in the neck was a calcified thyroid cyst or adenoma. Both lobes of the thyroid gland were enlarged, and the trachea was definitely indented by the cyst, as was usual in thyroid swellings.

**Hindquarter Amputation for Sarcoma.**—DUNCAN C. L. FITZWILLIAMS, C.M.G., F.R.C.S.

D. R., male, aged 62. This patient was shown at the meeting on October 11, 1937,<sup>1</sup> having a sarcoma in the groin and soft tissues of the thigh (fig. 1a).

On 19.10.37 a hindquarter amputation was performed and the specimen is shown (fig. 1b; fig. 2). It was originally intended to leave the ischial tuberosity for the



(a)

FIG. 1.

(b)

patient to sit on, but half-way through the operation it was discovered that the growth had burrowed through the ham into this region. The plan of the operation had, therefore, to be altered, with consequent loss of time. The patient had a transfusion during the operation, and the operation itself took thirty-five minutes; he stood it well and had two subsequent transfusions and some saline.

The pathological report was as follows:—

“Rhabdomyosarcoma of vastus internus. The tumour had a most interesting histology; it showed great pleomorphism and contained definite striated muscle cells” (figs. 3 and 4).

A small piece of the ileum remained and the symphysis pubis, to which was attached

<sup>1</sup> *Proceedings*, 31, 9, Clin. Sect., 1.



FIG. 2.



FIG. 3.—Rhabdomyosarcoma of *vastus internus*,  $\times 175$ .

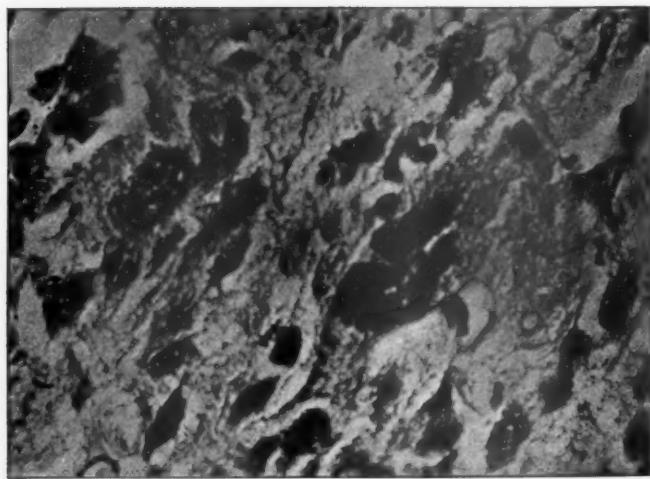


FIG. 4.—Rhabdomyosarcoma of *vastus internus*,  $\times 700$ . Note striations in cells.

the stump of the tendons of the abductor muscles. The sloughing of these tendons is the cause of the delay in healing, but nevertheless the patient is up and about.

He is the oldest recorded patient to undergo this operation.

**Extensive Squamous Carcinoma of Tongue.** — DUNCAN C. L. FITZWILLIAMS, C.M.G., F.R.C.S.

J. P., male, aged 57, stoker. Admitted to St. Mary's Hospital on 10.1.38, giving a three-years' history of having had "something wrong with his tongue", and difficulty in speaking and in eating.



J. P. Carcinoma of tongue.

On examination the condition shown in the photograph was found. There was an extensive carcinomatous ulcer spreading over both halves of the dorsum of the tongue, reaching almost as far back as the epiglottis ; it seemed to be quite superficial and no enlarged glands could be felt.

On 14.1.38 interstitial radium was given—a total dosage of 6,552 mgm.-hrs., and the result is the complete disappearance of the growth.

**Specimen of Carcinoma of Tongue Secondary to a Primary Growth in a Bronchus.**—DUNCAN C. L. FITZWILLIAMS, C.M.G., F.R.C.S.

J. R. R., male, aged 58. Admitted to St. Mary's Hospital on 25.11.37, having a swelling on the left side of the tongue. This had first been noticed in May 1937. It had disappeared at one time but at the end of September 1937 it reappeared at the same site. There was a history of two "fainting attacks"—the first in July 1935, when the patient said he vomited blood, and the other in the early part of 1937.

Examination revealed the condition shown in fig. 1. The tumour was about 4 cm. long, 2.5 cm. across, and was raised 1.5 cm. above the surface of the tongue on the left side, at the junction of the posterior and middle thirds. The submaxillary glands were large and hard. There was dullness over the chest and absence of air entry at the right base.



FIG. 1.—Case of carcinoma of bronchus: Secondary deposits in tongue.

On 30.11.37 interstitial radium was applied to the tongue; total dosage 1,410 mgm.-hrs. Interstitial radium was also given to the submaxillary region; total dosage 1,571 mgm.-hrs. The tumour on the tongue disappeared one week after treatment.

X-ray examination of the chest on December 3 suggested right bronchial carcinoma ; glands causing collapse by pressure on bronchus could not be excluded. Paracentesis of the right chest withdrew blood-stained fluid.

On December 10 biopsy of the tongue and of a gland removed from the right axilla showed an unusually malignant neoplasm, the cells being in parts polygonal, but in most places spindle-shaped, with hyperchromatic nuclei. There were large necrotic areas. The general appearance was unlike that of carcinoma of the tongue, but resembled that of bronchial carcinoma (see figs. 2 and 3).

The patient's cough became troublesome and clubbing of the fingers developed

rapidly. The sputum was scanty and did not contain blood. On December 14 there were râles all over the chest and there was a swinging temperature. Death occurred on 23.12.37.

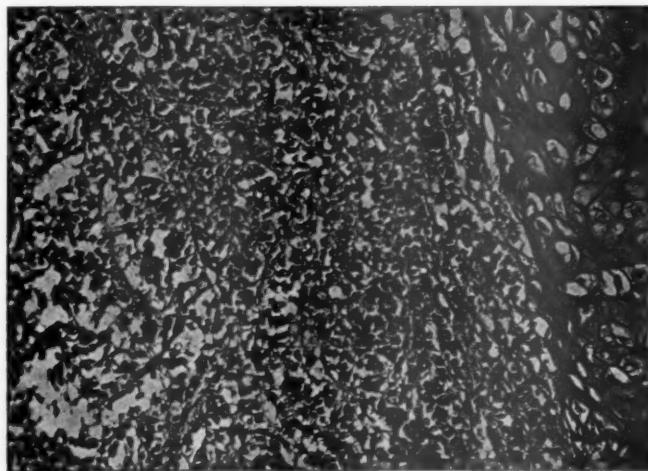


FIG. 2.—Carcinoma invading the cartilage of a bronchus.

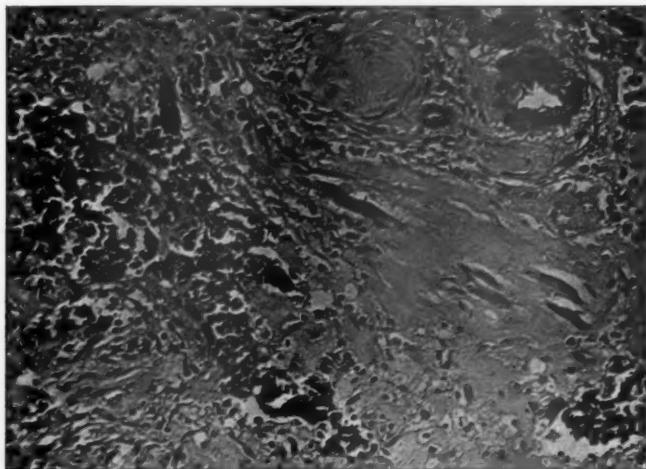


FIG. 3.—Secondary bronchial carcinoma in the tongue : after radium.

*Post-mortem findings.*—Bronchopneumonia of right upper lobe. Oat-celled bronchial carcinoma and bronchiectasis were found in the right lower lobe. Secondary growth was present at the hilum, in both axillæ, and in the deep cervical glands and in the glands of the epigastrium. Metastases were also found beside the right coronary artery and in the tongue.

**Secondary Metastases following Carcinoma of the Breast.**—DUNCAN  
C. L. FITZWILLIAMS, C.M.G., F.R.C.S.

A. J., female, aged 41, admitted, in July 1930, to St. Mary's Hospital, where her left breast was amputated on account of carcinoma. There was a twelve-months' history of tumour. The amputation was followed by application of radium 13,311 mgm.-hrs.

In February 1935 the patient returned for examination, having a swelling in the right breast and enlarged glands in the axilla. The glands were removed for diagnostic purposes; they were found to be carcinomatous; 11,938 mgm.-hrs. interstitial radium were given to the breast. At this time there was commencing proptosis and oedema of the left eye.

In February 1936 the patient was again admitted to hospital. Small nodules were felt, one over the right breast and one in each axilla; these were all excised. Those in the axillæ proved to be glands in which no carcinoma was found. The small piece of skin from the right breast, however, was found to contain polygonal-celled carcinoma. A radium plaque was applied to the glands above the clavicle on the left side, and 1,986 mgm.-hrs. were given.

Mr. Willoughby Lyle sent the patient to me again with the diagnosis of a secondary mass in the left orbit; this was confirmed by Mr. F. A. Juler. Interstitial radium was applied to the orbit, round the globe and through the sphenomaxillary fissure. As a result there was complete loss of sight in the left eye; either the optic nerve or the retinal artery must have been injured.

In June 1936 there were attacks of vomiting and epigastric pain; these passed off. In October 1936 small nodules appeared in the abdominal wall, above both clavicles and on the head. The nodules in the abdominal wall and those above the clavicles were treated by radium (small plaques, i.e. "brooches") 7,305 mgm.-hrs. being given; radium (1,235 mgm.-hrs.) was applied to the scalp. All the nodules disappeared.

In November 1936 greatly enlarged glands were present in both axillæ; these disappeared after the application of interstitial radium 1,430 mgm.-hrs.

The patient was readmitted in January 1938 with vomiting and epigastric pain; she thinks there had been slight loss of weight. X-rays show that she has a pyloro-duodenal obstruction, probably due to old cicatricial duodenal ulcer rather than to secondary new growth. Tiny nodules can still be faintly felt in the subcutaneous tissue.

The question now arises whether, in view of the obvious blood-borne carcinomatosis, it is worth while opening the abdomen and dealing with the duodenal obstruction.

Dr. GILBERT SCOTT: The treatment of multiple metastases by radium is a hopeless task. No sooner have one set of nodules been destroyed than others show themselves. The most satisfactory method to adopt in these cases is the wide-field X-ray therapy—an X-ray bath in which the whole trunk is subjected to rays of medium penetration, in small doses. Patients may, in this way, be kept alive and comfortable for several years.

**Subcutaneous Movable Spherules in the Ehlers-Danlos Syndrome.**—  
F. PARKES WEBER, M.D., and JANET K. AITKEN, M.D.

This is the patient, Mrs. M. B., aged 34, whose case was described in the *Lancet* (1938 (i), 198), as a peculiar example of the Ehlers-Danlos syndrome, the remarkable feature of which is the presence of freely movable subcutaneous nodules or "spherules", especially in regions where the skin is loose (*cutis laxa*); the atrophic, "papyraceous" scars, which constitute the most important sign in most cases, are very few in the present patient. Over-extensibility of joints is best marked at the proximal interphalangeal articulations. There are no gross abnormalities apart from those of the Ehlers-Danlos syndrome.

The spherules in question are mostly less than pea-sized and situated on the forearms and backs of the hands, where they can be easily shifted for an inch or more in any direction, without causing the patient any pain or discomfort. A few especially small ones about the right patella are strikingly hard to the touch. One from the back of the left hand was excised and found to be a fat-lobule enclosed in a firm fibrous capsule. Probably small subcutaneous lobules, after almost losing their pedicles and blood supply and with thickening of their capsules, develop into the characteristic freely movable spherules, which may afterwards become minute oil-containing cysts, with thickened fibrous or even calcified capsules. This throws light on supposed calcification of fat-lobules. It is possible that they also occasionally occur in cases which are not obviously examples of the Ehlers-Danlos syndrome. They should not be termed lipomata, but seem rather to represent a deviation in the normal fat growth—the arborescent (bud-like) development of freely movable lobules from the subcutaneous fat. It is possible that the pathological process in the rare so-called "arborescent lipoma" of joints is to some extent analogous.

In regard to family history the patient tells us that her parents were first cousins, and that her eldest daughter has over-extensibility of fingers and knees.

The abnormally developed fat-lobules in this case may perhaps be compared to various peculiarities which are known sometimes to occur in other tissues and organs: minute dense, sclerotic patches in bones; the minute so-called fibromata of the renal medulla (quite harmless); the occurrence of a percentage of peculiar corpuscles in the blood of members of some families (sickle-shaped, pear-shaped, oval or globular erythrocytes, "Pelger" leucocytes).

#### A Member of an Acholuric (Spherocytic) Jaundice Family described in 1910.—F. PARKES WEBER, M.D.

The patient, Mrs. Alice B., when I saw her in 1909, was aged 32 years, and was distinctly jaundiced. The spleen could be felt four fingerbreadths below the costal margin. The liver was apparently not enlarged. Blood-count: Hæmoglobin 70%: erythrocytes 3,520,000; leucocytes 4,750 (of which 78.2% were polymorphonuclear neutrophils); a few nucleated red cells were present. The resistance of the erythrocytes to graduated hypotonic sodium chloride solutions was decidedly below the normal, haemolysis commencing with the 0.64% solution. The blood-serum was abnormally yellow; it gave a negative Wassermann reaction. She stated that the jaundice had been accentuated during her pregnancies. Her father, aged 53 years, a younger sister, aged 14 years, and a brother, aged 12 years, were likewise typical subjects of familial acholuric (haemolytic) jaundice. Her father's father, who had died at the age of 76 years, had been yellow all his life. These family cases were described by me, with my then house physician, Dr. (later Professor) G. Dorner, in the *Lancet*, 1910 (i), 227.

The patient continued to enjoy fair health and to do her work as a market saleswoman till November 1932 when, as the result of a fall from a ladder, she sustained an intracapsular rupture of the spleen, which was removed at St. Bartholomew's Hospital (November 16) by Mr. J. E. H. Roberts (an urgency operation). She has since been free from jaundice.

Her sister and brother, mentioned above, and two of her grandchildren have likewise undergone splenectomy at St. Bartholomew's Hospital, with good results.

*Discussion.*—Mr. J. E. H. ROBERTS said that after incision of the peritoneum a dark, fluctuant swelling was seen; this was an encysted collection of old blood within the capsule of the spleen on its anterior aspect. The peritoneum over it gave way while being handled. A large quantity of old liquid blood flowed out into the peritoneal cavity, from which it was removed. The upper pole of the spleen was densely adherent to the diaphragm, and therefore

the pedicle of the spleen was first ligated and divided, and the spleen, which was of a very firm consistency, was removed intracapsularly in its upper part, leaving the capsule adherent to the diaphragm. The patient made a good recovery without incident.

In 1928, he (Mr. Roberts) had operated on three sisters of another family: Annie, aged 24, had developed a yellow colour at the age of 14, and had been yellow ever since. Mary, aged 14, was born yellow, and had been yellow ever since. Margaret, aged 12, was also born yellow. In each case there was an enlarged spleen; each sister had gall-stones, which were seen in the radiograms, and all three had a concretion in the appendix. In all there was greatly increased fragility of the red cells. In all three cases the operations of splenectomy, cholecystectomy, and appendicectomy, were performed at the same sitting, and in the case of the two younger girls on the same afternoon. They all made excellent recoveries without incident, and were known to be well four years later. Unfortunately they belonged to a rather poor family, and having migrated from the town in which they lived, had been lost sight of. Their mother said there were no similar cases on her side of the family, but that the father was yellow, had an abdominal tumour (presumably the enlarged spleen) and had had an operation for gall-stones. She could not give any information as to family or relations.

Dr. PARKES WEBER said he had recently seen a girl, aged 21 years, with familial acholuric (spherocytic) jaundice and gall-stones. The "fragility" of her erythrocytes was so great that haemolysis commenced with the 0.7% sodium chloride solution—in fact, with the most concentrated test-solution which had been prepared. She had contracted a prolonged, febrile stomatitis, which was followed by a terrible subacute painful rheumatoid arthritis of the hands, feet, and knees. The heart was not involved and there was no enlargement of any of the superficial lymph-glands. He (Dr. Weber) had never seen or heard of any similar complication in cases of acholuric jaundice.

In his experience some of the worst cases of the disease were those (especially seen in children) in which there was anaemia with splenomegaly, but no obvious jaundice.

The families which he had known illustrated, from the genetic point of view, obvious Mendelian dominance, such as had been observed in most recorded families.

Gall-stones in this disease were easily discovered by skiagrams, owing to their calcium-content. They should always be looked for before operation, as they were said to become an important complication in as many as 60 per cent. of all cases.

#### Congenital Acholuric Jaundice, without Anaemia, Splenomegaly, or Fragility of Red Corpuscles.—F. PARKES WEBER, M.D.

I first saw the patient, G. T. D., a man, now aged 71, in 1917 (*Proc. Roy. Soc. Med.*, Clinical Section, 1917, 10, 13). Excepting for considerable, somewhat variable, jaundice, chronic deafness (old otosclerosis) and slight nystagmus, he has always given the impression of an active, hard-working, healthy, elderly man, and has never been seriously ill, though at one time he suffered from an ulcer of the leg. Apart from the jaundice and a very strongly positive indirect Hijmans van den Bergh reaction in his blood-serum, he has presented none of the ordinary signs of congenital acholuric (haemolytic) jaundice. He has had no enlargement of the spleen or liver, no anaemia, no excessive "fragility" of erythrocytes, no excess of urobilin or urobilinogen in the urine, and there is no family history of jaundice or anaemia. Blood-Wassermann reaction negative. No microscopic abnormality of blood-cells has been discovered.

#### Case described as Acquired Acholuric (Haemolytic) Jaundice in 1909.—F. PARKES WEBER, M.D.

The patient, Mrs. L. W. (formerly L. P.), was first admitted to hospital in January 1908, when she was 39 years of age. She had begun to look pale three years previously and two years before admission she had had an attack of jaundice with pain in the right side. Blood-count (January 1908): Haemoglobin 18%; erythrocytes 900,000; C.I. 1.0; leucocytes 6,000 (eosinophils 0.8%; basophils 0.4%; polymorphonuclear neutrophils 46.0%; lymphocytes 45.6%; monocytes 7.2%); 8 megaloblasts and 16 normoblasts were seen during the count of 500 leucocytes; poikilocytosis; anisocytosis; polychromasia; basophilia punctata; no myelocytes (Dr. A. E.

Boycott). "Fragility" of erythrocytes was (doubtfully) very slightly in excess of the normal. There was a sub-icteric tinge. The spleen was greatly enlarged, reaching almost to the anterior superior iliac spine, and the liver was somewhat enlarged. An ordinary Ewald's test-breakfast showed absence of free hydrochloric acid. The great improvement which subsequently took place could not with certainty be attributed to the arsenical treatment (atoxyl); most of it took place after the arsenical drug in question had been discontinued (see *Trans. Med. Soc. Lond.*, 1908, 31, 389).

Later on I felt inclined to regard the case as one of acquired acholuric (haemolytic) jaundice with an "anaemic breakdown" associated with intense "megaloblastic regeneration" and great splenomegaly (cf. F. P. Weber, *Amer. Journ. Med. Sci.*, 1909, 138, 24).

But in 1923, during an anaemic relapse, I showed the patient at a meeting of the Section of Medicine (*Proceedings*, 1923, 16, 73), when Dr. William Hunter, after a careful review of the data available, expressed himself in favour of the case being one of pernicious anaemia. It should also be mentioned that in 1912 the patient suffered from an attack of interstitial keratitis in the right eye, but the blood-Wassermann reaction has mostly been completely negative. For further details see *Proc. Roy. Soc. Med.*, 1927-1928, 21, 80.

In 1928 Mr. John Elgood at the Hackney Hospital successfully removed the gall-bladder with a large number of stones in it, and also removed the appendix, which was bound down by adhesions.

Liver diet was at first used somewhat irregularly, but with the steady use of a liver extract patient has remained free from anaemic relapses. At present she has no jaundice and no anaemia, and neither spleen nor liver can be felt enlarged. She can do her housework easily. Brachial blood-pressure: 140/90 mm. Hg. Blood-count: Haemoglobin 80%; erythrocytes 4,950,000; leucocytes 6,750 (eosinophils 3%; polymorphonuclear neutrophils 63%; lymphocytes 28%; monocytes 6%); thrombocytes 290,000; no abnormal red cells. I presume that complete gastric achylia (even with histamine control) is still present, as it was in 1931 and again in 1932, when last tested for by the fractional method.

From the *symptomatic point of view* the case is an example of recovery from a severe disease at one time presenting a clinical picture which might be termed: "Severe acholuric (haemolytic) jaundice with great splenomegaly and a megaloblastic blood-crisis."

**Arthritis of Lumbar Vertebral Articulations.**—ERNEST FLETCHER, M.B.

H. F., male, aged 59, tram conductor.

*Past history.*—1916: Was involved in an accident; he was in a tram-car which fell over, and he temporarily lost consciousness.

August 1921 to July 1922: Pain in back. Treated in hospital for two months. Diagnosis: Lumbago affecting the spine.

*History of present condition.*—Has had similar pain since July 1937. Left leg gives way. Says he "cannot stand the 'speeding-up' on the trolley-bus", and that he has lost 6 lb. recently.

*Family history.*—Negative.

*On examination.*—General condition fair. Blood-pressure 164/86. Back: Fibrosis of both glutei. Spine: Moves badly and is tender all the way up; at the level of D. 11-12, the vertebral spinous process is very prominent. X-rays show considerable calcification to the right of the spine, which on lateral view is shown to be confined to the area posterior to the vertebral discs.

Sedimentation rate: 5 mm. at one hour.

Dr. GILBERT SCOTT said that the bone changes in the spine might be an atypical form of Paget's disease and suggested radiological examination of other bones.

**Spondylitis Ankylopoietica, with Infective Focus Round Sacro-iliac Joints.**—ERNEST FLETCHER, M.B.

L. M., female, aged 39.

*Past history.*—Rickets as a child. 1927: Difficult labour, due to ? contracted pelvis; forceps were applied, but the baby died. Some pain in left shoulder during pregnancy and afterwards. After the puerperium there was pain over the sacrum and back of the neck, and the patient could not walk for a month.

1930: Two miscarriages. 1933: Labour induced at 8 months. Has worn a ring pessary since.

*Present condition.*—Complains of back being "set" for three years; cannot turn her head to the side or bend it backwards; is stiff when walking, but is better by day than by night; has pain at lower end of spine and in the hips.

*Family history.*—Mother had rheumatic fever.

*On examination.*—General condition good. Teeth deficient; right lower molar carious. Central nervous system normal. Blood-pressure 148/92. Spine: cervical, no lateral, and very little anteroposterior, movement; dorsal and lumbar, tender, and with poor movement.

X-rays show an infective spondylitis, with an infective focus round the sacro-iliac joints.

Sedimentation rate varies from 40 to 11 mm. at one hour.

*Treatment.*—April to July 1937: 0.18 grm. solganol B oleosum. A slight improvement has taken place.

Dr. GILBERT SCOTT: This case is evidently one of active spondylitis ankylopoietica—a better name is spondylitis adolescens, as the disease only attacks the young healthy adult. I have at present under review the histories and radiograms of about 350 cases of this disease, all of which show signs of chronic infection of the sacro-iliac joints (chronic sacro-iliitis). The active stage of sacro-iliitis is indicated clinically by recurrent attacks of wandering rheumatic pains from five to seven years before the onset of spinal symptoms. For this reason, there is now a rule at the British Red Cross Society's Clinic for Rheumatism that all patients under 25 accepted for treatment must submit to an X-ray examination of the sacro-iliac joints. We are now for the first time seeing the early stages of spondylitis ankylopoietica, or spondylitis adolescens. Wide-field X-ray therapy is used in all these cases with remarkably good results if treated in the early, or active, stages.

**Coarctation of Aorta and Congenital Phlebarteriectasis of Left Arm.**  
—D. EVAN BEDFORD, M.D.

Male, aged 33, first seen 10.12.37.

*History.*—No rheumatic fever, chorea, or syphilis. When aged 17 he first noticed that the left arm was longer than the right. From 1933 to 1935 he was doing manual work and at times the left arm ached. Early in 1936 he injured the middle finger of his left hand, which became painful and discoloured, but eventually improved. In April 1937 he was in hospital in Manchester, with gangrene of the left middle finger. In November 1937 the left arm became very painful and prevented him from working, and the finger became worse.

*Examination.*—Pulse regular, rate 95. Blood-pressure (right arm) 205/105 mm., falling with rest to 170/80 mm. No enlargement of heart. No murmurs.

X-ray examination: Notches on the 5th-9th ribs characteristic of coarctation of aorta. No enlargement of heart. In the left oblique position, the site of constriction of the aorta can be seen. Electrocardiogram: Normal.

In the interscapular region dilated vessels can be felt, and a systolic murmur is audible. Femoral pulsation is diminished.

The left arm is purplish, and all the superficial veins are enlarged and distended. The left forearm is  $1\frac{1}{2}$  in. longer than the right. The left brachial, radial, and ulnar arteries are dilated and tortuous. Expansile arterial pulsation is felt in the left

hand and fingers. There is gangrene of the tip of the left middle finger, and decalcification of the phalanges.

Arteriography of left arm (Mr. Ascroft) : The injection passed rapidly into the veins ; the radiographs show tortuous dilated vessels in the fingers.

Dr. PARKES WEBER said he regarded the (apparently unique) association of coarctation (stenosis of the aortic isthmus) with the "haemangiectatic hypertrophy" of the left arm as an example of the association of two kinds of congenital or developmental abnormality in the circulatory system, analogous, for instance, to the association of coarctation of the aorta with congenitally weak spots in the arteries at the base of the brain, leading to the development of so-called (often wrongly-called) "congenital" aneurysms.

He regarded the gangrene in the finger of the left hand as of ischaemic origin and due to arterial thrombosis occurring in abnormally developed vessels, cutting off the blood supply (compare thrombosis occurring in varicose veins). As to treatment, he could not give his opinion at once.

## Section for the Study of Disease in Children

President—T. TWISTINGTON HIGGINS, O.B.E., F.R.C.S.

[January 28, 1938, continued]

**A Boy Exhibiting Nervous Symptoms ascribed to Kernicterus with Septic Neonatal Jaundice as Cause.**—REGINALD LIGHTWOOD, M.D., and T. COLVER, M.B., Ch.B., M.R.C.P.

E. M., aged 2 years 10 months, was brought to hospital one month ago because he was still unable either to speak or to walk.

**History.**—A first child. Pregnancy, labour, and delivery normal. Full-term baby; weight  $7\frac{1}{2}$  lb. He appeared to be quite healthy until the fourth day of life when the umbilicus became inflamed. Next day there was a purulent discharge which persisted until the eighteenth day. Jaundice was present on the eighth day and persisted for twelve weeks. During this period there were three convulsions, each lasting for a few minutes. The umbilical cord separated on the twelfth day. Progress after disappearance of jaundice seemed satisfactory. The child did not sit up, however, until the age of 10 months, and was unable to stand, even with support, until aged 2 years 8 months. The parents believe that he is perfectly intelligent. His habits are clean, he plays with toys, is affectionate, and crawls about the house.

**On examination.**—General: Rather a small boy (weight 28 lb.). Can sit up; is observant, and co-operates during examination. Movements unsteady and clumsy. There are also involuntary movements of the head, trunk, and limbs; these are short and jerky, neither choreic nor athetoid; they are emphasized during voluntary movement. He does not speak. He can propel himself along the floor, his arms doing most of the work; with the support of a chair he can just drag himself to a standing position. Eyes: Coarse nystagmus; pupil reactions normal; fundi normal. Limbs: slight rigidity.

Nervous system: Tendon reflexes all present and normal; abdominal and cremasteric reflexes brisk; plantar reflexes equivocal. No demonstrable impairment of sensation; it is impossible, in this child, to investigate fully all the forms. Heart, lungs, and abdomen: Normal.

**Investigations.**—Blood Wassermann reaction of patient and mother negative. Skiagram of skull normal. Muscle electric reactions: No gross abnormality.

**Comment.**—The nervous symptoms seen in this patient consist of extrapyramidal rigidity and disturbances of motility, with cerebellar inco-ordination but no mental deficiency. That they are due to kernicterus is suggested only because there is a clear history of prolonged neonatal jaundice; this was septic in origin.

In this country and in America kernicterus has been regarded, hitherto, as a sequel peculiar to grave familial jaundice of the newborn, but C. de Lange (1924) has, on clinical grounds, suggested that it may follow septic jaundice as well. Recently, proof of her belief has been supplied from autopsy material by Biemond and Creveld (1937). For some reason not yet known, it seems that in immaturely developed brains, the barrier between blood and cerebrospinal fluid may be more permeable to bile pigments (and perhaps to toxins). Such (cerebral) tissue-immaturity is put forward as an explanation why kernicterus occurs in some jaundiced neonates but not in all.

### REFERENCES

LANGE, C. DE (1924), *Acta paediat.*, **4**, 60.  
BIEMOND, A., and CREVELD, S. VAN (1937), *Arch. Dis. Childhood*, **12**, 173

? Schizophrenia beginning at about 3 years of age : Case for Diagnosis.  
—I. YATES, M.D.

S. M., male, aged 11 years, attended the Queen's Hospital for Children, December 20, 1937, on account of frequency of micturition. There was a history of psychological symptoms beginning between the ages of 3 and 4 years.

*Family history.*—No history of psychosis, psychoneurosis, or mental deficiency obtained. No consanguinity of the parents. Patient is the third of four surviving children.

*Personal history.*—Born 15.8.26. Normal birth. Stood at 12 months, walked at 14 months, said single words at 15 months, was beginning to say sentences at 18 months, clean at 18 months. Attack of measles at 3 years and 4 months; kept in bed for two or three weeks. Subsequently an abscess developed in the neck and he was in the Mile End Hospital three weeks. No history suggesting an attack of encephalitis obtained. His mother dates his mental illness from that time, although he did not see a doctor with regard to psychological symptoms until after he had attended school when 5 years old. Before the age of 3 years he had played normally with other children; he was "full of mischief", and showed initiative, but was said to have been destructive with his toys. Some time between 3½ and 5½ years various symptoms developed, though the actual date of onset is very difficult to place. His mother says that when he was 5 years old he was constantly talking to himself in an incoherent fashion. He was very restless, was frightened of strangers and animals, often shaking with fright when at school and crying to go home. At 5½ years he had fits of temper if he could not get what he wanted. These occurred for about two years.

*Abstract of Report from London County Council:* At 4 years 9 months first attended school; excluded after five months because of extreme instability. Mental testing of this boy was extremely difficult. At 5 years and 10 months his mental age seemed to be about 3 years; he was extremely garrulous, with irrelevant speech. Dr. Levinson of the East London Child Guidance Clinic reported him to be in a state of phantasy and recommended a special school which would "help to bring him into more touch with reality". Attended M.D. school from age of 6 to age of 10 years. At 6 years and 9 months, mental age was about 3½ years; at 7 years and 5 months, about 4 years; at 8 years and 5 months, nearly 5 years; at 10½ years his mental age was just above 5 years, with much scattering. He was throughout recognized as not an ordinary case of amentia.

*Present state.*—Expression varies; sometimes vacant. Is restless and talks constantly to himself in disjointed sentences or single words, referring largely, apparently, to past happenings. Shows echolalia and perseveration. His mother thinks she can always connect up his utterances, but her explanations sometimes seem to need the use of her own imagination. He laughs to himself, and grimaces, especially in front of a looking-glass, but no evidence of delusions or hallucinations was obtained. If left to himself he takes some notice of his surroundings. He will carry out simple commands, e.g. he undresses himself easily when asked, and will fetch and carry for his mother, but his attention quickly wanders and he continues chatting to himself. He is no longer miserable or frightened, but gives an impression of cheerfulness. His mother says: "He gets upset if I am upset", showing that his emotions are still affected by reality. His habits are clean.

Intelligence quotient 51; mental age 5 years 10 months. (Revised Stanford-Binet scale.) Owing to difficulty in sustaining his attention this is only approximate.

*Physical examination.*—General physical condition good. Tendon reflexes brisk. "Variable left internal concomitant strabismus; no evidence of paresis of any extra-ocular muscles. Fundi normal; fields full so far as it is possible to ascertain" (Mr. E. F. King). Physical examination otherwise negative. Wassermann reaction negative. Urine normal.

*Comment.*—The patient shows withdrawal from reality and appears to live in a world of his own ; as one cannot get into contact with his world it is impossible to say what his various utterances mean. His world is very circumscribed, but that is to be expected, since his mental defect is marked and his emotional development is, I think, not more than that of a child aged 2 years. In the course of half a minute he said in the consulting room, "Going home now—puff puff—Easter egg—sluice—take that home ?" (pointing to a toy motor car). "Getting a big boy now, getting locked up—Easter egg—." One seems justified in concluding that he is capable of forming various concepts. "Sluice", for example, definitely did not refer to anything in the immediate present. It is a word he is reported to have been saying one or two years ago, and taking this in conjunction with observations made at the East London Child Guidance Clinic, I think it has reference to a phantasy. His mother's explanation was that he connected the word with hospitals and she thought he must have been told, in a previous hospital, that he would be put down the sluice.

*Diagnosis.*—Amentia, that is congenital mental defect, can be ruled out on the history. The mother gives, in the main, a good history, which has been corroborated at various points. She had had three children previously and she is certain that in this case early development was normal. As there is no evidence of any organic lesion of the central nervous system, and no history of intracranial infection or injury, or of fits, we may exclude meningitis or brain tumour, &c. There remain, it seems to me, two possible causes of the dementia : (1) A slowly progressive schizophrenia ; (2) a measles encephalitis at the age of 3½ years, which so affected the boy's cerebrum that it was incapable of normal development. With regard to the latter, no history of encephalitis was obtained either from the mother or from the records of the case during the time he was in the Mile End Hospital just after the attack of measles. However, not wishing to diagnose schizophrenia, owing to its rarity at this patient's age, I went through some of the literature on measles encephalitis in the hope of finding some similar case. Mental deficiency may follow measles encephalitis. Ford (1928), who gives a summary of the literature up to 1928, states that "the commonest mental residuum of measles is a reduction in intelligence", and again (1937) in his recent book "Diseases of the Nervous System in Infancy, Childhood and Adolescence" he says : "In my experience the disseminated encephalomyelitis of measles and chicken-pox very frequently causes some degree of mental deficiency although rarely complete idiocy." He says that he has been struck by the profound changes in personality which have followed measles encephalitis. But I could find no case with severe residual mental defect yet without clear evidence of an organic lesion, at least in the acute stage, nor have I found any record of a child living in phantasy after measles encephalitis. I exclude the time of mental confusion which may be associated with the acute or early convalescent stage. In view of all these facts there seems very little to support a diagnosis of measles encephalitis.

I would therefore diagnose this as a case of schizophrenia, though I admit it is a bold diagnosis. Lutz (1937), writing in 1937 in the *Swiss Archives for Neurology and Psychiatry*, was able to find in the literature only 14 undoubted cases of schizophrenia beginning under the age of 10 years. To these he added six cases of his own. He takes 10 years as the dividing line between the schizophrenia of adults and adolescents and that of children. Bleuler, who introduced the term schizophrenia, takes 15 years as the dividing line, and says that only 4% of his cases started under 15 years old. Lutz agrees with Homburger that to make a diagnosis of schizophrenia there must be evidence of deterioration of the personality. He considers that in children there are two types of the disease : (a) The slowly progressive, without marked remissions—as in this boy—and (b) a type often accompanied by catatonia, which is of comparatively sudden onset, with definite exacerbations. The main characteristic of the adult schizophrenic is his increasing withdrawal from his environment ; he is self-absorbed to the exclusion of actuality ; there is loss of unity between thinking, feeling, and

conduct. For instance a patient may say she is Queen of England but she makes no effort to conduct herself accordingly nor does it bother her that she is not clothed according to her status. The schizophrenic may have various symptoms, such as delusions, hallucinations, catatonia, ideas of reference, &c., but none of these are diagnostic of schizophrenia. As Henderson and Gillespie (1936) say, "if we wished we could form as many groups as there are individuals". There is nothing diagnostic of schizophrenia in this boy's echolalia, grimacing, and restlessness. These are present in many idiots, and are normal in infants, although in a much less marked degree.

I think that the diagnosis of schizophrenia is justified in this case by the withdrawal from reality and the failure in development of normal emotion, conduct, and thought. At 11 years he has a "mental age" (using a technical term) of 5 years or thereabouts, but a considerably lower level of emotional control and of mode of thought.

I am much indebted to Dr. Emmanuel Miller for giving me particulars of the boy's mental state when he attended the East London Child Guidance Clinic. I also wish to thank Dr. Helen Mackay for referring the case to the Psychological Clinic.

#### REFERENCES

FORD, F. R. (1928), *Bull. Johns Hopkins Hosp.*, **43**, 140-184.  
 Id. (1937), "Diseases of the nervous system in infancy, childhood and adolescence", London.  
 HENDERSON and GILLESPIE (1936), "Textbook of psychiatry", London.  
 LUTZ, J. (1937), *Schweiz. Arch. f. Neurol. u. Psychiat.*, **39**, 395-372.  
 Id. (1937), *ibid.*, **40**, 141-161.

*Discussion.*—Dr. W. S. MACLAY: It is difficult for a psychiatrist to help Dr. Yates in the diagnosis of this interesting case. Firstly, because so little is known about psychoses in very young children, and secondly, because the conception of schizophrenia varies so much among different people. It seems clear that this case is not one of primary amentia, but it may possibly be one of interrupted development due to measles and encephalitis. The normal development in the first three years may explain why the picture is not that of typical congenital mental defect, and, of course, its diagnosis as due to the after-effects of encephalitis does not preclude the possibility of such a patient showing certain schizophrenic symptoms.

Dr. C. W. Vining said that this was a very unusual case and certainly not one of congenital inborn mental deficiency. The mental aspect of the boy was quite in keeping with the diagnosis suggested—namely schizophrenia. He thought, however, that the possibility of encephalitis following an attack of measles could not be excluded as the cause of the mental condition.

The symptoms of encephalitis at the time of the attack might be extremely slight yet the result might be extremely devastating.

#### Two Cases of Infantile Myxœdema, with X-ray Findings.—REGINALD C. JEWESBURY, D.M.

I.—P. D., female, now aged 9 years (figs. 1, 2, 3).

Previously shown on October 22, 1937 (see *Proceedings*, 1937, **31**, 75, Sect. Dis. in Child., 7).

II.—R. L., female, aged 5½ years.

*Complaint.*—Lack of growth.

*Family history.*—Father and mother well and of normal habitus. One sibling died aged 18 months.

*Past history.*—Birth-weight 8½ lb. Breast-fed for nine months. Sat up at 10 months. First tooth at 11 months. Began to talk when aged 18 months. Pertussis, May 1937.

*History of present illness.*—Has not grown properly since age of 3 years. Appetite poor. Child constipated. Stated to be nervous but intelligent, and goes to school.



FIG. 1 (P. D.).—Delayed ossification in carpal bones.



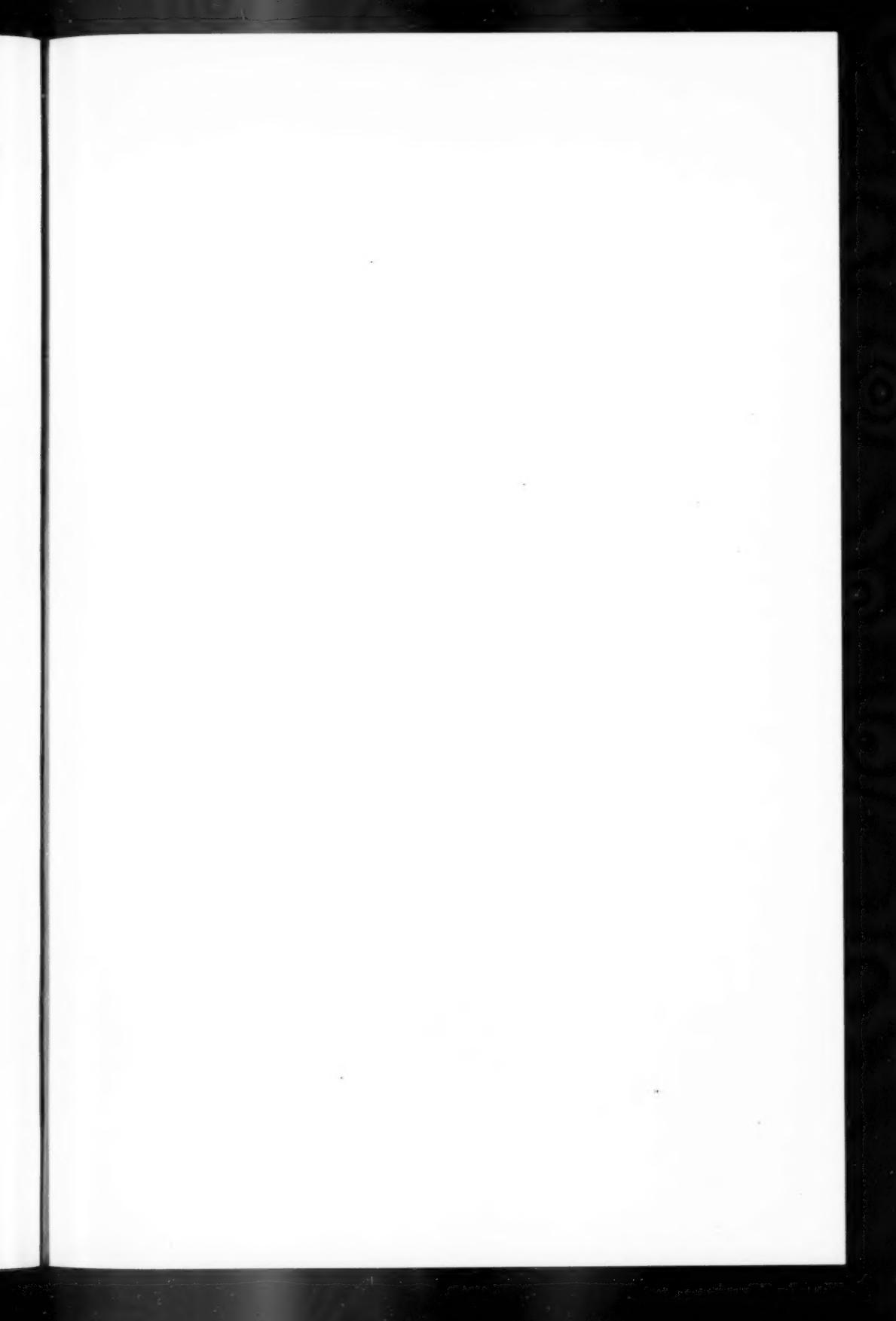
FIG. 2 (P. D.).—Stippled fragmented epiphysis of femur (before treatment). -



FIG. 3 (P. D.).—After treatment with thyroid extract for three months.



FIG. 4 (Case II).—R. L., 5½ years. Showing stippled fragmented epiphyses.



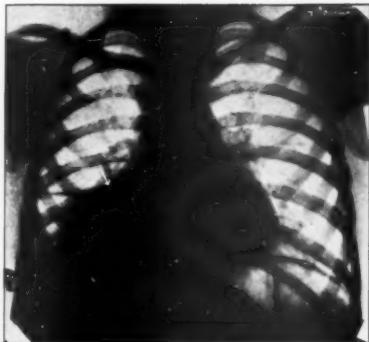


FIG. 1.  
FIG. 1 (9.12.35).—Triangular basal shadow (indicated by arrow). Middle lobe clear but displaced downwards.



FIG. 2.  
FIG. 2 (13.12.35).—Middle and lower lobes opaque.

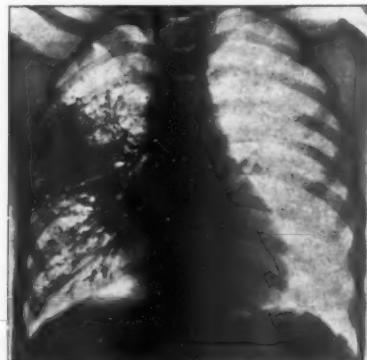


FIG. 3.—Bronchography performed after lung signs had cleared: appears to show slight indentation of right bronchus by a large calcified gland (indicated by arrow).

*State on admission.*—Temperature 97° F.; pulse 120; respiration 26. Small child. Stands with marked lordosis. Measurements: Height 34½ in. Height from pubis to soles 15 in., and vertex to pubis 19½ in. Weight 32 lb. 14 oz. Circumference of head 20½ in., thorax 21½ in., and abdomen 22½ in. Hair rather sparse, not unduly brittle. Skin rough and sallow. Features coarse; bridge of nose sunken. Tongue normal. Teeth very good. Neck short. Supraclavicular regions full. Abdomen prominent. No umbilical hernia. Heart and lungs normal. No thyroid palpable. Mentally very slow indeed. Quite lethargic and stays in whichever position she is placed. Will not answer questions, but does not resent examination.

X-ray examination: Skull: Normal sella turcica. Wrists: Delayed epiphysis and abnormal ossification at epiphyseal lines. Hips: Stippled fragmented epiphysis (fig. 4). Shoulders: Stippled epiphysis. Dentition: Normal.

Blood-count: R.B.C. 4,110,000; Hb. 75%; C.I. 0.9; W.B.C. 11,500. Differential: Polys. 47%; lymphos. 43%; large hyals. 9%. B.M.R. 32%.

*Treatment and progress.*—Given thyroid ¼ gr. t.d.s. 11.1.38: Dose of thyroid increased to ⅓ gr. t.d.s. The temperature has been persistently subnormal, but the child has brightened considerably and has become quite lively.

Dr. LIGHTWOOD, after referring to the pathological work of Langhans (1897) concerning the multiple ossific centres which form in the epiphyses of cretins, said that descriptive reviews of the epiphyseal changes characteristic of cretinism and juvenile myxoedema had appeared in German literature (von Seemen, 1928; Loeser, 1928), and recently, Reilly and Smyth (1937) had redescribed them. The epiphyses, especially the capital epiphyses often formed from multiple centres of ossification, giving rise to a "stippled" appearance. Slowly—but more rapidly under treatment—the multiple loci fused, but the epiphyses remained irregular in shape and their radiological appearance might come to resemble the destructive changes seen in Calve-Legg-Perthe's disease. Some (not all) untreated cretins showed these changes in the capital epiphyses.

*References.*—LANGHANS, T. (1897), *Virchow's Arch. f. path. Anat.*, **149**, 155; VON SEEMEN, H. (1928), *Arch. f. klin. Chir.*, **152**, 616; LOESER, E. (1928), *Lehrbuch der Röntgendiagnostik*, Georg Thieme, Leipzig, 362 (quoted by Reilly and Smyth); REILLY, W. A., and SMYTH, F. S. (1937), *J. Pediat.*, **2**, 786.

**Recurrent Lobar Collapse.**—DOUGLAS GAIRDNER, B.M. (by courtesy of E. A. COCKAYNE, D.M.).

Stanley N., male, aged 8½ years, was first seen when aged 4 years, having a history of cough intermittently ever since an attack of bronchopneumonia when aged 3 years. His father had died from chronic pulmonary tuberculosis a year previously.

1.8.33: Present cough followed a cold two weeks before. Temperature, pulse, and respirations normal. Lungs: Dullness, tubular breathing, râles and bronchophony over right middle and lower lobes. X-ray examination (Dr. Bertram Shires, No. 1): Right middle and lower lobes opaque, ? slight displacement of heart to right, group of small calcified glands near the right hilum. W.B.C. 13,000, with 73% polymorphonuclears. Mantoux reaction positive; stomach washings injected into a guinea-pig with negative results for tuberculosis. Lungs: Signs rapidly cleared and cough disappeared.

20.11.33: Cough returned, one week. Lungs: Coarse râles right base. X-ray examination No. 2: Right base clear, except for opacity in cardiophrenic angle; septum between upper and middle lobes thickened. Heart central.

20.4.34: Cough returned three days. Temperature 100.2° F. Appeared ill but had no respiratory embarrassment. Lungs: Signs identical with those on 1.8.33.

31.12.34: Cough returned. Temperature 100.4° F.; respirations increased. Lungs: Signs over right middle and lower lobes as on 1.8.33. 5.1.35 (Skiagram No. 3):

Similar to No. 1 ; 22.1.35 (No. 4) : Right base nearly clear. Large calcified gland close to trachea ; position also seen from lateral skiagram (No. 5).

12.8.35 : No symptoms or signs. Skiagram showed large calcified gland and thickened interlobar septum as before ; otherwise clear.

5.9.35 : Unwell for five days past ; abdominal pains ; night sweats, but no cough. Temperature, pulse, and respirations normal. Lungs : Recurrence of tubular breathing &c. at right base ; these signs persisted for a month, nevertheless the child remained fit and gained weight (no skiagram taken).

9.12.35 : Cough five days. Temperature, pulse, and respirations normal. Skiagram No. 6 (fig. 1) : Triangular shadow suggesting collapse of right lower lobe ; middle lobe clear but displaced downwards ; heart probably displaced to right. Both antra radiologically opaque. Skiagram No. 7 (fig. 2), four days later : Opacity spread to the middle lobe. Sputum : Pus cells ++, staphylococci and *Friedländer's bacillus*. Signs rapidly cleared. 30.12.35 Skiagram No. 8 : Lower lobe cleared, but some shadowing persisting in region of middle lobe. ? partial collapse of middle lobe.

During the next two years the child was well, except for occasional coughs ; the lungs remained free from abnormal signs.

22.11.37 : Severely ill for one week, with cough and noisy breathing. Temperature : 100° F. Skiagram No. 9 : Opacity suggestive of pneumonic process spreading out from right hilum towards base. 29.11.37 : Condition unchanged, respirations 56. Lungs : Over right middle and lower lobes, dullness, tubular breathing, râles, aegophony, and pectoriloquy ; over left lower lobe, dullness, bronchial breathing, and bronchophony. Skiagram No. 10 : Right middle and lower lobes opaque (appearance resembling that in Nos. 1 and 3) : Opacity at left base suggestive of pneumonia. 4.12.37 : Child now well. Skiagram No. 11 : Left base clear, right as before. 14.12.37 (Skiagram No. 12) : Both lungs now clear.

*Other investigations.* — Bronchogram No. 13 : Large calcified gland in angle formed by trachea and right bronchus ; bronchial tree normal (fig. 3). Wassermann reaction negative. Sedimentation rate normal. Antral wash-out revealed pus in one antrum. Bronchoscopy (Mr. James Crooks) failed to show any abnormality of the bronchi as far down as the main bifurcation of the right lower lobe bronchus.

## Section of Psychiatry

President—E. GOODALL, C.B.E., M.D.

[January 11, 1938]

### Cardiazol Convulsion Therapy in Schizophrenia

By L. C. COOK, M.B.

THROUGH the good offices of Professor Golla and the Mental Hospitals Committee of the L.C.C., I was able this summer to visit Budapest, where the treatment of schizophrenia by induced convulsions was originated by Dr. Lazlo Meduna in 1934. Meduna introduced this method because he believed that there was a biological antagonism between epilepsy and schizophrenia. Whether this is really the case is a debatable point, and the treatment must as yet be considered as entirely empirical. It undoubtedly constitutes, however, a safe and convenient form of severe shock therapy, which is at least as effective as any other known method.

For many years it has been well known that any severe shock, whether in the nature of acute physical illness or of intense physiological stimulation, occasionally produces dramatic improvement in cases of schizophrenia. More recently insulin shock, and now induced convulsions, have shown themselves capable of producing similar benefit. Despite intensive research, the metabolic changes inherent in schizophrenia are quite unknown, but it is evident that they are not irreversible and that these shock methods are sometimes able to reverse them. It is possible that researches into the metabolic changes brought about by hypoglycemia and by convulsions may be more fruitful, and may be able to throw some much-needed light upon the original errors.

Convulsion therapy was first introduced in the form of intramuscular injections of a 25% camphorated-oil solution. Meduna, however, soon discovered the immense advantages of intravenous cardiazol. Cardiazol (pentamethylene tetrazol), a synthetic water-soluble compound, is primarily a cardiac and respiratory stimulant, and its uses in this capacity are, of course, well-known. For convulsion therapy it is convenient to use a 10% aqueous solution, made up freshly every two or three days, sterilized by autoclaving at 110° C. for twenty minutes and kept in air-tight, rubber-capped bottles. Stronger solutions are unnecessary and are liable to cause severe local reactions.

*Dosage.*—Doses as small as 0.2 grm. may be sufficient to produce a fit, but 0.5 grm. (5 c.c. of the 10% solution) is the usual initial dose. This amount is always quite harmless, and to start with it often saves time and material. The same dose is administered as long as it produces a major fit. When the initial dose fails to produce a convulsion or when at any time during the course a fit fails to occur, an increase of 0.1 grm. is given at the next injection. In practice a few increases are often found necessary during a course. Thus a patient whose first fit may have followed the injection of 0.5 grm. may be needing 0.8 grm. by the time 20 fits have been induced. Few patients need more than 0.7 grm. to produce their first fit. Of 42 female patients, 33 had their first fit after the injection of 0.5 grm., three after 0.6 grm., one after 0.65 grm., four after 0.7 grm., and the remaining one after 0.8 grm. When once the effective dose is reached, approximately 85% injections, discounting failures due to technical mishaps, should be successful. One of my patients has had a course of 28 fits, during which the dosage only had to be raised to 0.7 grm., while another has had 24 successful injections with the minimum dose (0.5 grm.). Meduna fixes a maximum dose of 1.6 grm., not because he considers larger amounts to be in any way dangerous, but because he thinks that a very bad prognosis attends such "fit-resistant" cases. I have never found it necessary to give more than 1.2 grm. as a single dose, but have immediately followed a subliminal dose of 1.1 grm. with a second injection of 1.2 grm., without any ill-effects except slight vomiting. In Dr. Meduna's opinion the provocation of fits with small doses denotes a good prognosis, but of my eight female patients, who have had unsuccessful courses, six needed only 0.5 grm. to produce their first fit.

*Course.*—Fits are usually induced every three days, but in some cases it may be preferable to give the injections every other day. In the event of an unsuccessful injection a further dose should be given immediately, but may be left until the following day. By "unsuccessful" is meant any injection that fails to produce a true major fit, as described later.

The length of the course depends on the individual subject. When improvement occurs, it may be dramatic in its rapidity, gradual, or fluctuating, and in some cases continues steadily for some weeks after the course has finished. When a full remission is considered to have been established during treatment, it is usual to give at least three further fits, in order to diminish the chances of relapse. In the event of incomplete remission 25 to 30 fits are generally taken to constitute a full course. In completely unresponsive cases 20 fits should be induced before the treatment is given up, but actually nearly all cases show some improvement within the first 15 fits.

*Technique.*—The technique is simple. No specially trained nursing staff, no prolonged observation, no imposing emergency table, and no anxiety is necessary. The injections are usually given between 11 and 12 o'clock in the morning not less than three hours after the patients have had their ordinary breakfast. They may, however, be given at any time, so long as the stomach is relatively empty. The injections are always given in a separate room, so that other patients can neither see nor hear anything of the procedure. Screening-off is insufficient, as screaming and other alarming noises may usher in or accompany the fit.

The solution is injected into one of the antecubital veins as rapidly as possible. The more suddenly the solution reaches the general circulation, the smaller is the dose needed to produce a fit. For this reason, unless the veins are small and tend to thrombose, fairly large needles ( $\frac{9}{10}$  mm. bore) are used, and the tourniquet is only loosened as the injection ends.

*The fit.*—The fit closely resembles a severe, spontaneous, generalized, epileptic convulsion, and shows all the characteristic phases. In parenthesis I would add that it affords an unprecedented opportunity to investigate epileptic convulsions under perfectly controlled conditions.

The time relations of the various phases of the fit have all been taken from the moment of the release of the tourniquet, which is effected suddenly and not until the end of the injection. By this means the whole of the fluid reaches the general circulation, in bulk as it were, at the same moment. The first sign, which is usually a fixing of the expression, occurs within five seconds of the release of the tourniquet. It is immediately followed by a short cough, blepharospasm, or twitchings round the mouth. Any combination of these signs may be noted, the cough occurring three to ten seconds, and the other two signs five to fifteen seconds, after the injection. The occurrence of a cough at three seconds suggests a vagal reflex initiated from the heart, as the solution can scarcely reach the brain within seven seconds.

The next phase is that of large, myoclonic jerkings of head, limbs, and trunk, which occur from eight to twenty seconds after the injection and usually last from two to ten seconds. This phase, however, may be only momentary or may last as long as half a minute. It is followed by a phase of generalized tonus, which constitutes the beginning of the major fit proper. It usually starts ten to thirty seconds after the injection and is always very severe. Its average duration is eleven seconds (three to twenty-five seconds), after which it merges into the clonic phase, approximately eighteen to forty seconds after the injection. The clonic phase lasts twenty to fifty-five seconds and is succeeded by a state of flaccidity fifty-five to ninety seconds after the injection. The flaccidity is sometimes interrupted by occasional generalized myoclonic jerkings together with momentary dilatation of the pupils. At the beginning of this stage respiration is slow and explosive, cyanosis may be evident, and the pulse, which is usually slightly accelerated, may sometimes be slow and occasionally irregular.

The pupils are nearly always dilated throughout the convulsive stages of the fit and the eyes often show extreme deviation to either side, even in the same patient. Spontaneous extensor plantar sign and "goose-skin" are frequently noticed. When micturition occurs, it usually accompanies the onset of the flaccid stage, but occasionally takes place at the end of the tonic phase. The tonic phase is ushered in by a long yawn, giving ample time for a tampon to be placed in the mouth. During tonus the limbs are usually fully extended. The arms may at first be raised above the head, to be slowly stretched down to the sides. Extreme pronation of the arms is not uncommon, and the thumbs are usually forced between the fingers. The wrists and fingers are nearly always tightly flexed, but one patient often assumed a typical clawhand position. During the clonic phase the forearms may become flexed and adducted. The legs are occasionally flexed at both knee- and hip-joints during tonus.

On one occasion, unique in my experience and in the literature, a typical fit occurred ten to fifteen minutes after the injection, long after all effects had apparently passed off. Quite recently, however, I have been informed by Dr. McCartan that he has observed two late fits five minutes and twenty-two minutes after injection. Any explanation of this rare phenomenon is beyond my powers. At this point it may be timely to mention that the occurrence of spontaneous fits, whether organic or functional, following a course of cardiazol, has never been observed.

When a major fit fails to occur, the initial signs usually appear, but invariably stop short of the tonic phase. Blepharospasm may be prolonged and there may be short, panting respirations, sighing, screaming, and even intense excitement. The myoclonic stage may last for over a minute, and cataleptic and other hysteriform phenomena may follow. The patient becomes inaccessible during the initial stages and there appears to be a concomitant loss of consciousness, which lasts from a few seconds to about two minutes.

*After-effects.*—The major fit is followed by a short period of coma, and complete consciousness is usually regained in from five to ten minutes. Recovery is sometimes

associated with confusion, restlessness, and mild excitement, lasting a few minutes, but most patients are quiet and soon drop off into normal sleep. In some emotional and unstable cases a longer period of over-activity and noisiness, conveniently treated with paraldehyde, may follow, while—very occasionally—intense excitement prevails. These symptoms may persist for as long as half an hour. The patients usually have their midday dinner in bed and get up afterwards, but any who prefer it or who are at all shaken by their experience stay in bed for the rest of the day.

Vomiting may occur, but if no meal has been taken for two or three hours before the fit, it is both infrequent and slight. It depends to some extent on the amount of cardiazol administered, as I have found a greater tendency to vomit after two injections have been given, the first one being subliminal. This accords with the experimental finding that cardiazol irritates the vomiting centre (Schwartz, 1928). Occasionally complaints of headache or of muscular pains are made, but these cause no serious inconvenience to the patients.

*Dangers.*—If due precautions are taken, danger is insignificant. Meduna has treated over 400 cases without any fatality, whilst in all upwards of 1,500 cases must have had cardiazol treatment. As far as I can ascertain, there have only been three deaths in connexion with these cases. Of these, two patients were obviously unfit for treatment, one suffering from severe aortic disease (Angyal and Gyarfás, 1936), and the other from double hypernephroma and goitre (Briner, 1937). The remaining death is reported to have been due to pulmonary embolism, following a long-standing pelvic thrombo-phlebitis (Briner, 1937). As regards our experiences at Bexley, my colleagues and I have induced over 1,400 major fits without encountering any really alarming features.

Respiration may momentarily cease in the flaccid stage of the fit, but pressure on the lower ribs immediately restarts it. Transient cyanosis is usual and may possibly be of therapeutic value. Occasional irregularity of the pulse occurs, but is quite temporary, and I have seen no tendency towards heart failure. Electrocardiographic examination before and after treatment has been made by Dobozy (reported by Meduna, 1937) and by Hadorn (1937), and both maintain that cardiazol treatment produces no ill-effects upon heart muscle. Naturally, a thorough physical examination should always precede treatment and all patients suffering from general bodily illness—especially of the heart and lungs—or any form of pyrexia, should be excluded. I have confined treatment to subjects under 40 years of age, but have successfully treated one patient who had had rheumatic chorea, and another who had had two fairly recent attacks of acute rheumatism.

Of minor accidents, dislocation of the jaw is not infrequent, but in only one of my cases was there any pain or swelling afterwards. Fractures and dislocations of limbs have been reported and I have met with one case of dislocated shoulder, which apparently resulted from a stretching movement during recovery of consciousness. The dislocation was very easily reduced and has not interrupted the course of treatment.

*Complications.*—(a) Fibrosis of veins: Although dangerous or serious sequelæ are conspicuously absent, two annoying complications tend to occur. The first is local fibrosis of the injected veins. This fibrosis only presents a problem in subjects whose suitable superficial veins are few and small. It seldom arises in males or in thin, muscular females, but in a number of fat or flabby young women in whom adequate veins are originally at a minimum, it may invalidate all available veins and so delay, or even prematurely terminate, treatment. It appears to be due to minute lacerations of the vessels and to penetration of the fluid into the wall itself. The fibrosis is not attended with any pain, and I have never seen any phlebitis or other complication. In many cases the fibrosis is not complete and if the vein is rested, the lumen may soon become re-established. Even so, treatment may be delayed

during the process of recovery, if there are few adequate veins. In the most severe cases the arm may present nothing but a few fibrous cords after a dozen injections, and I have been ironically congratulated by some of my less seriously-minded colleagues on discovering a new substance for the treatment of varicose veins. In order to minimize this disadvantage great care must be taken to ensure that the point of the needle is free in the lumen of the vein, a matter of no difficulty where veins are large and conspicuous, but not so easy where they are "thready" and tend to run away from the point of the needle. It is helpful to use steeply bevelled needles with thin walls, but as speed of injection is so important a factor, the lumen of the needle must be fairly large. It is said that a 20% cardiazol solution is definitely irritating to the vessel wall and that serious local thrombosis may follow its use. The advantages of using a solution weaker than 10% would, I think, be outweighed by the disadvantages enforced through having to inject much larger volumes of fluid. It is possible that modifications in the constitution of the solution may eventually render it completely non-irritant, but damage to vessel walls *per se* is liable to provoke a reaction. The use of a buffered solution, made up by adding 0.01 grm. % di-sodium hydrogen phosphate, has been advocated, but after an extensive preliminary trial of this, I am now using a simple aqueous solution (pH 7.7), such as is used at Budapest. On the whole I have experienced less trouble with venous fibrosis since using the aqueous solution, but I attribute this more to improved technique than to the fluid itself. Although this feature is not of frequent occurrence, it has already delayed treatment in the case of several improving patients, who relapsed badly during their rest, and has stopped treatment altogether in one promising case.

(b) Distress: The second disadvantage is the distress sometimes produced by the treatment. A few patients go through a course without any marked dislike of the procedure, but the majority soon grow to fear the injections, and a few reach a pitiable state of apprehension and alarm. Fortunately, means of reducing this complication to a minimum are now at hand. The distress is mainly associated with non-fit-producing injections, which often beget an indescribable feeling of dysphoria and frustration. It can be lessened by giving an immediate sedative, which must not be an anti-convulsant, such as luminal, as this tends to prevent the occurrence of a fit next day. Following Meduna's more recent practice, however, it is now our habit to give a second and larger dose immediately after an unsuccessful injection, thus reducing to a minimum the period of distress and saving time in the course of treatment. Apart from the distress caused by subliminal doses, definitely alarming sensations are experienced in the few seconds between the end of the injection and loss of consciousness. These sensations are remembered better by some patients than by others, but most have a vague but urgent memory of their unpleasant nature. They appear to be peculiarly terrifying and are sometimes associated with visual hallucinations. Several patients associate them with anaesthesia; one always begs me not to give her "this gas or ether", whilst another once said "It is as if I were going off under an anaesthetic and just not going—left half-way as it were—an awful feeling". Some liken the sensation to "electricity all over me", and most agree that it affects the whole body, but especially the head and chest. The head may feel "all on fire", and there is often a feeling of pressure and suffocation around the thorax. Some of the more picturesque descriptions have been: "The ceiling all jumps"; "It is like air being pumped into my body all over—I feel all blown out"; "They make me feel as though a great big policeman was jumping on top of me".

Dr. Rees Thomas, who recently visited Budapest, informs me that efforts are being made there to shorten the prodromal period by adding vasodilator substances to the solution injected. It seems doubtful, however, if any significant mitigation will be obtained by this means, as the average duration of conscious distress is probably less than ten seconds.

The question of premedication with sedatives has naturally been considered from the beginning. I first tried the effect of paraldehyde upon patients who showed definite fear of the injections, and found that 2 drm. produced little alleviation of their distress, while 4 drm. necessitated much larger (sometimes even double) doses of cardiazol. Hyoscine hydrobromide was found to have little or no effect upon the amount of cardiazol required, but was not altogether successful as a sedative. For the last fortnight I have been using hyoscine and morphia in combination, with the result that severe apprehension and distress have become a thing of the past. The administration of morphine sulphate  $\frac{3}{8}$  gr., hyoscine hydrobromide  $\frac{3}{250}$  gr., and atropine sulphate  $\frac{1}{100}$  gr., half to three-quarters of an hour before the injection in no way diminishes the patient's susceptibility to fits and effectively damps down the severest manifestations of alarm. The actual dose of sedative is, of course, modified to the needs of individual patients.

The only method of completely eliminating distress so far evolved is that of combining insulin and cardiazol therapy and administering cardiazol during insulin coma. In these circumstances the patient's susceptibility to convulsions is increased and smaller doses of cardiazol are effective. This procedure is used extensively by Müller and others in Switzerland, and has been applied in this country by Russell.

*Spontaneous remissions and results of treatment.*—Statistical results of treatment in schizophrenia rest on far too fluid a basis to be of any scientific value, and even spontaneous remission figures show the widest variations. The worthlessness of such estimates taken as a whole is evident from Table I, which was shown by Dr. H. Pullar Strecker in the course of a recent paper on insulin therapy, and which I am using with

TABLE I.—SPONTANEOUS REMISSION FIGURES IN SCHIZOPHRENIA.

Author	When published	Total	Cases Traced	Ratio in percentage				Period under review
				Well or improved	Not improved	At mental hospital	Died	
Lemke	1935	192	48	14	29	9	1933/35	
Faurbye	1936	72	42% more or less recovered					1935
Meyer-Gross	1929	328	294	35	3.4	19	42.5	1912/13
Lemke	1935	255	126	34	19	27	20	1918/23
Otto-Martiensen	1921	527	312	33.7	7.4	21.1	31.4	?
Otha	1936	?	179	29% complete remission				?
Dussik	1936	94	20%					?
Arnesen	1937	815	772	18.5% " recovered				1915/28
Menzies	1935	17		5.9%				1928/30
Stearns	1912	?	915	5	4.5	64.1	23.8	?
Ederle	1937	147		3.4% complete remission				1935
Total	...	2,460		23.6%				

his kind permission. The remission percentages, as taken from only 11 studies, vary from 3-4% (Ederle) to 48% (Lemke). It is obvious that these figures will depend on a number of variable factors. First, the diagnosis of schizophrenia is by no means an easy or an exact one. Secondly the length of time elapsing between the period under review and the time of the follow-up investigation will naturally affect the results. Thirdly the standards of recovery, remission, &c., are individual to each compiler of results. The average spontaneous remission rate for unselected cases of all types and durations of schizophrenic illness is given by Müller (quoted by Ellery, 1937) as probably being between 15 and 20%. This estimate appears to be as near the mark as is possible to judge.

Treatment figures suffer from the same disadvantages, whilst they are further vitiated by selection of cases. This may affect the figures either way, but indicate

more accurately the standards of the investigator than the value of the treatment. If only the most favourable cases are selected, a good prognostician should be able to produce a recovery rate of over 90% with either insulin or cardiazol. If early cases are given a chance to recover spontaneously, before treatment is started, the remission figures will naturally suffer. This is the usual practice at Bexley, as it is obviously unjustifiable to give a course of shock therapy to all newly admitted schizophrenics, some of whom may remit spontaneously in a short time. If all cases are treated indiscriminately, the results will depend upon the type of material available, the remission percentage naturally varying inversely with the number of chronic cases. For this reason it is usual to divide tables arbitrarily into cases of under and over one year's duration. It is well known that spontaneous remissions occur very much less frequently after the first year of the disease, and it will be seen that treatment results show a similar tendency.

TABLE II.—COLLECTED RESULTS OF INSULIN AND CARDIAZOL TREATMENT.

Author	Duration of illness												
	Under 1 year			1 to 2 years			Over 1 year			Over 2 years			
	Non-remissions	remissions	Total	Rem.	N.-r.	T.	Rem.	N.-r.	T.	Rem.	N.-r.	T.	
<i>(Insulin)</i>													
Müller (1937)	... 162 (57%)	121	283	24 (27%)	64	88				14 (11%)	110	124	495
Dussik and Sakel (1936)	73 (70%)	31	104										104
Küppers (1937) (collected)	39% full remissions							7% full remissions					962
<i>(Cardiazol)</i>													
Meduna (1937)	... 89 (91%)	4	43	9 (50%)	9	18				6 (12%)	43	49	110
Angyal and Gyarfas (1936)	12 (44%)	15	27				5 (28%)	13	18				45
Briner (1937)	... 20 (59%)	14	34				8 (10%)	70	78				112
Küppers (1937) (collected)	59% full remissions							2% full remissions					262

I am prefacing my own figures with a table of collected results of a number of workers with both insulin and cardiazol. The contrast in results between cases of under one year's duration and those of over two years' duration is clearly seen throughout the table. Where the schizophrenic illness has existed for less than a year, the remission rate for insulin varies between 39% and 70% and for cardiazol between 44% and 91%. When the illness has lasted over two years, remissions are in the neighbourhood of only 10%. The remission rate for both forms of shock therapy can, I think, fairly be taken as at least twice as great as that to be expected from spontaneous remission. In addition, recovery is definitely more rapid and saves considerable hospitalization.

*Personal results.*—I have tried to make my own remission criteria conform to that of other workers, particularly Müller and Meduna, whose tables show the largest number of cases treated with insulin and cardiazol respectively. By "recovery" I mean that patients have been discharged and are back at their previous occupation or, in a few cases, are on trial or waiting to be discharged. They have lost every trace of schizoid feature and have gained good insight. In "very good" or "social" remissions, I include those who are as well as they were before their illness—at their individual best. By "great improvement" I mean really great improvement, such as a change from stupor or catatonic excitement, with dirty habits, &c., to a state of being able to look after their needs and work usefully in the hospital. This group is chiefly made up of cases of over three years' duration. In my opinion all these cases would definitely be placed by Müller and by Meduna in their "remission" column. Certainly the treatment has changed them out of all recognition.

TABLE III.—CARDIAZOL. BEXLEY HOSPITAL, 1937.

Duration of illness	Recovered	Very good or social remission	Great improvement	Slightly improved	Not improved	Total
Under $\frac{1}{2}$ year	3	1		1	1	5
$\frac{1}{2}$ to 1 year ...	2		1		1	4
1 to $1\frac{1}{2}$ years	4	2		1	1	8
$1\frac{1}{2}$ to 2 years				1	1	2
2 to 3 years		1	4		7	12
Over 3 years	2	1	3	2	6	14
Total	11	5	8	5	16	45
<i>Summary</i>						
		Remissions		Non-remissions		Total
Under 1 year	...	7 (79%) [6 (67%)]		2	...	9
1 to 2 years	...	6 (60%) [6 (60%)]		4	...	10
Over 2 years	...	11 (42%) [4 (15%)]		15	...	26
Total	...	24 (53%) [16 (35%)]		21	...	45

[Figures in square brackets denote recoveries or very good remissions.]

So far 45 patients at Bexley Hospital have had completed courses of cardiazol. The results in general are approximately equal to those of other workers, while those of old-standing cases are considerably better than any previously published. Unlike many others, we have found little difference in result whether the illness has been of under six months' duration or between six months and one year, but of course our material is too small for this to be of any significance. A remission rate of six out of 10 cases of between one and two years' duration compares favourably with the experiences of others. Our greatest triumphs, however, have been gained with some of those supposedly almost intractable schizophrenics whose illness has lasted more than two years. Of 26 cases two have been discharged as recovered, two have very good remissions, and seven have shown striking improvement. If these 11 patients, with their histories, had been shown to you before the discovery of shock therapy, I am certain that even the most cautious of you would have been prepared to give very long odds against their chances of significant improvement. These cases alone make cardiazol treatment worth while trying in any mental hospital.

Far more trustworthy than statistical tables, at any rate at this early stage, are the impressions of experienced clinicians and nurses. I add nurses because they are less inclined to be carried away by the glory of administering a new treatment and because the distress occasioned to some patients tended at first to bias their opinions against cardiazol. Now they are enthusiastically in favour of it and spontaneously suggest cases for treatment. As regards the medical staff, we at Bexley have no doubt as to the value of this form of therapy.

Early cases: As one would expect, complete recoveries mainly attend, but are by no means confined to, early cases of acute onset. Of these, stuporose and confused types are generally agreed to have the best prognosis.

The most dramatic recovery I have encountered was that of a young school teacher, who was admitted in a state of severe hallucinosis and confusion and of extreme terror. She imagined that a war was raging around her and that all her relatives were killed. At my approach she screamed with terror, thinking I was going to cut her up into specimens. A course of somnifaine was given at first, partly owing to her pitiable condition and partly because convulsions were temporarily contra-indicated owing to a spinal injury. After a course of prolonged narcosis she gradually fell into a semistuporose state, but remained vividly hallucinated and gravely apprehensive. Whilst in this condition four months after the onset of her illness, her first cardiazol fit was induced. Twenty minutes later she was asking in a dazed way where she was. On the following day she was up and knitting. She received two more fits, made an uninterrupted recovery, and is now back at her work. This girl might well have recovered spontaneously in time, but no one can doubt that

convulsion treatment precipitated her recovery or that it saved her many months of hospital detention.

Even in recent and acute phases recovery is not usually so sudden, and in one case it was interesting to see during the course of treatment a stage of stupor giving place to one of fatuous irresponsibility, which itself slowly cleared up, leaving a normal personality.

Paranoid types are said to offer considerable resistance to cardiazol therapy, but if of recent and rapid onset, they are by no means intractable.

A young married woman was admitted with a short history of paranoid ideas and auditory hallucinations. She was mildly confused, devoid of insight, and convinced, quite unjustifiably, of her husband's infidelities. She needed only 13 fits to effect a complete recovery with restoration of excellent insight, and she is now managing her household normally and happily.

Less success attends the treatment of early cases of schizophrenic excitement, especially when the predominant affective state is one of elation. This may be partly due to the tendency for cardiazol to produce a mood of euphoria and spurious confidence together with slight press of ideation—in fact a state of hypomania. This stage is seen in most cases, but is transient and gradually passes off after the end of the course. Cardiazol, perhaps for this reason, has a beneficial—although not always a lasting—reaction upon anxious, apprehensive, and diffident schizophrenics, and its effect upon selected cases of non-schizophrenic anxiety and depression is now being tried.

The outlook in hebephrenia is thought to be fairly good by Meduna, but poor by most other workers. I have had insufficient results to pronounce any opinion. In cases of simple apathy, as opposed to stupor, the prognosis is definitely poor, but this syndrome is usually of gradual onset and shows no "florid" stage. As Dr. Meduna has observed, the prognosis is incomparably better if the treatment is given while the patient is in a "florid" state. This is undoubtedly true, but, nevertheless, mode of onset and previous personality prove more reliable prognostic guides than does symptomatology. An insidious onset coupled with a personality which has always been introverted, "peculiar", or "difficult", suggests a very poor prognosis, whatever the symptoms may be. Hereditary factors do not appear to influence the immediate prognosis nearly as much as the foregoing factors, but, of course, further attacks are more likely to occur.

Passing to the consideration of cases of more than a year's duration, the results of insulin or cardiazol treatment show an obvious superiority over those to be expected from spontaneous remission. A good example of recovery after cardiazol therapy in a patient, whose expectation of spontaneous remission was remote, is that of a 19-year-old girl, who was admitted to Bexley Hospital in September 1936. Her conduct and general attitude had been abnormal for some months and acute symptoms had set in towards the end of August. Cardiazol treatment was not begun until she had been in the hospital for nine months, and her illness had lasted well over a year. Throughout her stay at Bexley she had been inaccessible and completely detached from reality. She was vividly hallucinated and expressed fragmentary delusions of a bizarre nature. She was wont to throw herself on the floor or impulsively strike her companions, giggling as she did so. Her habits were shamelessly dirty, her clothes always torn and untidy, and she required every nursing attention. She improved slowly, but steadily, throughout her cardiazol course. After nine fits she was accessible and interested in her surroundings. She occupied herself, and looked after her needs, but was still hallucinated, giggled a good deal, and had no insight. A total of 21 fits was given, after which she talked rationally, behaved normally, realized that she had been ill, and was grateful for her treatment. She was discharged without any schizophrenic tendency and is now at home leading a normal life.

**Chronic cases:** When a schizophrenic illness has already lasted three years or more, complete recovery is extremely rare, yet perhaps the most striking results of cardiazol are seen in such cases. Here, again, stuporose and vegetative subjects of catatonic type fare best, and I think it may fairly be claimed that cardiazol fits can always interrupt a state of stupor. Occasionally it may be replaced by catatonic or even maniacal excitement, but usually stuporose subjects are rendered accessible, amenable, and useful.

One of my first patients treated by cardiazol was a young woman, who had remained in a state of complete stupor, except for the exhibition of occasional impulsive acts, for three years. Throughout the day she soaked herself with saliva and other excretions and, of course, required hand-feeding and every nursing attention. She is now a useful worker and looks after all her needs. She is, it is true, simple and childish, without insight and prone to periodical phases of emotional excitement, which, however, react immediately to a further two or three fits. Other semi-stuporose subjects have shown more stable improvement, but I have never seen so dramatic a metamorphosis after so long a phase of stupor.

**Relapses.**—A tendency to relapse, as exhibited by this woman, is not infrequent in cases of incomplete remission and can easily be counteracted by a few further convulsions. If treatment is interrupted before completion, relapse is common, and the control of progress by stopping and restarting treatment gives convincing proof of the direct effect of the convulsions. On only one occasion have I met with a definite relapse during the course of uninterrupted treatment. This occurred rapidly and for no apparent reason in the middle of steady improvement, but I am glad to say the patient is now remitting well again.

Post-convulsional lucidity with a tendency to relapse within forty-eight hours has been observed in two cases of agitated, resistive stupor. In one, treatment was at length given up, as the periods of lucidity gradually diminished in length until they existed for no more than half an hour. In the other, periodical batches of fits are still being given, as they are now successful in maintaining the patient's accessibility for several weeks in succession. Relapses after treatment are common in patients who have only made a partial recovery. They usually occur from one to four weeks after cessation of treatment, and can nearly always be cut short by a few further fits. Some of these patients have had a number of short courses after their original treatment. They tend to improve more and more each time, but complete remission has so far eluded them. After the establishment of a full remission I have not yet seen a relapse, but naturally they are to be expected, as in the case of spontaneous remission. They have been reported by several writers, after both insulin and cardiazol, and have usually been successfully dealt with by a second course of treatment.

**Recurrent cases.**—Good results have been obtained in recurrent cases, although they may not have achieved more than a "social" remission over a period of several years. One patient with recurrent schizophrenia, whose original breakdown occurred at least four years ago, has been recently discharged as recovered after a course of cardiazol. Both he and his mother state emphatically that he is now far better than at any other time since the origin of his illness, and that at last he has really recovered. This completeness of recovery is an important feature of shock therapy in general. Müller (1936) has observed that recovery after insulin is both quicker and more complete than in spontaneous remission, and I find the same happy result in cardiazol recoveries.

**Importance of adjvant treatment.**—Although the mode of action of any form of shock therapy is unknown, the first and probably the most important clinical change is the re-establishment of accessibility and contact with reality. This must be immediately seized upon and taken advantage of vigorously and persistently. Cardiazol should be accompanied and followed up by energetic occupational therapy

and psychotherapeutic advice and encouragement. This appears to help in accelerating improvement and in preventing relapse in partially remitted cases.

Whenever possible, patients are kept in the hospital for at least a month after the end of the course and no claim of recovery is made before this period has elapsed.

*Cardiazol in relation to other therapeutic methods.*—Lastly I should like to touch briefly on the subject of cardiazol in relation to other forms of treatment. I do not think that any but prolonged narcosis and insulin need be considered. The former in its modern form was introduced in 1920 by Kläsi (1922) who, I believe, still prefers it to any other method of treating schizophrenia. In this country very fair results have been published by Ström-Olsen (1934), Parfitt (1936), and Palmer (1937), but Müller (1925), whose experience and judgment are entitled to the greatest respect, obtained real improvement in only one out of 19 cases. Seven of my patients had a fortnight's course of somnifaine narcosis before cardiazol was tried. Two, who were in a state of severe catatonia, showed no change after narcosis. One of them is now making considerable progress under cardiazol, but the other had a full cardiazol course without improving. In four others, all of whom were agitated and distressed, somnifaine produced some alleviation of symptoms, which did not last more than four days in any case. Two of these achieved the same condition after two or three fits, and later made further improvement, but both have relapsed and are not likely to make permanent remissions. The other two are recent cases and are both improving satisfactorily with cardiazol; one, in fact, is in a state of remission after five fits and should make an excellent recovery. In the remaining case, which has already been described, cardiazol effected a dramatic recovery after somnifaine narcosis had failed. None of these cases was more than transiently improved by prolonged narcosis. Even when cardiazol achieves no better results than narcosis, its effects in my experience are more rapid and not so transient.

Insulin and cardiazol should be regarded not as rival, but as complementary, methods of treatment. Their statistical results are similar, but insulin appears to have a curative predilection for paranoid and excited syndromes, while cardiazol produces its best results in states of confusion, stupor, and distress. In ideal circumstances both methods should be available. Patients may then have either or both at the physician's discretion. The combined method abolishes the distress associated with cardiazol, whilst retaining the beneficial effects of regular convulsions. In Vienna the practice of giving cardiazol after improvement has been obtained with insulin appears to be very successful, partly, I suspect, owing to the euphoria produced by cardiazol.

Cardiazol has the advantages of a simple technique, necessitating no large or specially trained staff, and of comparative freedom from danger. The dangers of insulin therapy, however, are rapidly decreasing as experience of its action accumulates.

#### REFERENCES

ANGYAL, L., and GYARFAS, K. (1936), *Arch. f. Psychiat.*, **106**, 1.  
 BRINER, O. (1937), *Schweiz. Arch. f. Neurol. u. Psychiat.*, **39** (Supplement), 118.  
 DUSSIK, K. T., and SAKEL, M. (1936), *Ztschr. f. d. ges. Neurol. u. Psychiat.*, **155**, 351.  
 ELLEBY, R. S. (1937), *M. J. Australasia*, p. 552.  
 HADORN, W. (1937), *Schweiz. Arch. f. Neurol. u. Psychiat.*, **39** (Supplement), 64.  
 KŁASI, J. (1922), *Ztschr. f. d. ges. Neurol. u. Psychiat.*, **74**, 557.  
 KÜPPERS (1937), Triennial Meeting of German Society of Neurologists and Psychiatrists Munich, Sept. 1937. Abstract in *Psychiat.-neurol. Wchnschr.*, **52**, 596.  
 MEDUNA, L. (1935), *Ztschr. f. d. ges. Neurol. u. Psychiat.*, **152**, 235.  
 Id. (1936), *Arch. Neurol. and Psychiat.*, **35**, 361.  
 Id. (1937), "Die Konvulsionstherapie der Schizophrenie", Halle.  
 MÜLLER, M. (1925), *Ztschr. f. d. ges. Neurol. u. Psychiat.*, **96**, 659.  
 Id. (1936a), *Nervenarzt*, **9**, 569.  
 Id. (1936b), *Schweiz. med. Wchnschr.*, **66**, 929.  
 Id. (1937), *Schweiz. Arch. f. Neurol. u. Psychiat.*, **39** (Supplement), 9.  
 PALMER, H. A. (1937), *J. Ment. Sc.*, **83**, 636.  
 PARFITT, D. N. (1936), *Lancet* (i), 494.  
 SCHWARTZ, A. (1928), *Comp. rend. Soc. de Biol.*, **21**, 222.  
 STRÖM-OLESEN, R. (1934), *J. Ment. Sc.*, **80**, 668.

[February 8, 1938]

## A Year's Experience of Insulin Therapy in Schizophrenia<sup>1</sup>

By G. W. B. JAMES, RUDOLF FREUDENBERG, and A. TANDY CANNON

WHAT is known as the insulin shock therapy of schizophrenia, introduced by M. Sakel in 1933 at the Pötzl Clinic, Vienna, has been in use at Moorcroft House, Hillingdon, since January 1, 1937. This communication summarizes the experiences of 1937, 24 cases being completed during the period.

The technique of the authors has been described in an article contributed to the *Lancet* (1937), which does not require any essential modification.

Throughout 1937 we have begun treatment at the hour of 7 a.m., and the total hypoglycæmic period has seldom been allowed to exceed five hours. In exceptional cases in which coma has arrived very late we have extended the period up to six hours. This means that interruption usually occurs at the latest at 12 noon, a time convenient for hospital administration, as it allows patients to be bathed and dressed and ready for lunch at the usual hour of 1 p.m.

From experience we believe it to be wise to drop the term "shock", because we feel that in some quarters there is a tendency to magnify the dangers of insulin therapy. Müller (1937) in a series of 495 cases treated in Swiss hospitals, gives the mortality rate as 0.5%, and it is probable that with improvement and standardization in technique this mortality rate may be still further reduced. With proper supervision and immediate access to the appliances necessary to deal with emergencies, very few are really alarming. We return later to this question, but would add here that it is easy to become lulled into a sense of security by the regular passage of days or weeks of treatment without incident. Emergencies come with dramatic suddenness, and fatalities would be certain were there any relaxation in vigilance or lack of essential appliances.

The brand of insulin has been varied. For the first six months we used a brand of pure crystalline insulin, changing at the end of this period to a gland extract. There has been no urticaria in the whole of our series, and no differences were observed in the effects of the two preparations.

*Dosage.*—Even after a year it is not easy to give any precise information about the average dosage of insulin required to produce hypoglycæmic coma. We aim at producing coma in the third hour of hypoglycæmia. Coma has been produced by 15 units, while another case required over 400 units. This wide variability in sensitivity to insulin is very striking, and dosage cannot be forecast with any accuracy. Insulin tolerance appears to vary in the same patient during the course of treatment, some patients developing an increased resistance, others an increased sensitivity. In the great majority of our cases, dosage has been decreased after the initial coma dose has been reached. For example, if the initial coma dose is found to be 100 units, that dose may be reduced to 90, 80, or even 70, units later in the treatment, to produce satisfactory coma. We agree with Müller (1937) that this variability in sensitivity bears no relation to mental improvement or the reverse.

*Effect of dosage on blood-sugar.*—Blood-sugar estimations that have been made show a fairly constant series of changes. Within an hour of the injection the blood-sugar falls to 30 mgm. per 100 c.c., or even less. It remains at about that level during the whole of the hypoglycæmic period. Half an hour after interruption, when

<sup>1</sup> A film was demonstrated at the meeting, divided into two parts; the first, showing the normal course of insulin therapy from injection to interruption in the same patient, the second consisting of "shots" of different patients showing the phenomena of hypoglycæmia.

the patient is conscious, the blood-sugar has risen to a little below normal; about one hour after interruption it has returned to normal, and continues to rise under the influence of the large carbohydrate supply.

*The order of appearance of neurological and psychological effects of hypoglycaemia.*—This subject has been carefully described and considered by Parfitt (1937), and our daily records in the main confirm his observations. Parfitt (1937) has stated that he saw no improvement as a result of insulin fits. Our observations on this point show that four patients whose symptoms had lasted up to eighteen months before admission definitely dated mental improvement from the occurrence of a single insulin epileptiform attack. We were so impressed by these observations that we used cardiazol in certain cases in addition to insulin, to induce epileptiform seizures. The cardiazol is now given one to two hours after the injection of the coma dose (Georgi, 1937). A small group of cases cannot justify the drawing of conclusions, but references are made to results in Table II. The criticism may, very properly, be made that it is impossible to know whether improvement has been due to insulin or cardiazol, as so many patients in our small series have had both. We continue to use insulin and cardiazol combined in selected cases, and incline to the view that the combination of the two methods may show better therapeutic results than either alone.

*The duration of coma.*—It is very essential that the daily length of coma be extended gradually, and not allowed to continue beyond a period at which the patient is found by experience to rouse easily after interruption and to remain free from after-effects. In any case deep coma should never be extended beyond a period of one and a half hours (Dussik and Sakel, 1936). This optimum length of coma depends chiefly on physical reasons: some patients seem built to stand lengthy comas which others are unable to tolerate.

*The interruption of hypoglycaemia.*—In our communication on the technique of insulin therapy (1937) we described the precautionary passing of the nasal tube when severe muscular twitchings, for example, suggested the imminence of an epileptiform fit. We have learned to drop this procedure, and if an epileptiform attack does develop we no longer interrupt intravenously, but pass the tube at the conclusion of the first fit, apparently with perfect safety. In our 24 cases we have had 73 epileptiform attacks due to hypoglycaemia: 14 of them were interrupted intravenously, and 59 by tube. We no longer regard an epileptiform attack as an emergency, and we mention this fact here as it modifies our former published view.

*Intravenous interruption.*—During 1937, with a total of 1,628 patient-insulin days, intravenous interruption was necessary on 106 occasions. Table I summarizes the reasons for intravenous glucose therapy. This total of 106 does not include the 14 occasions on which intravenous glucose was used to interrupt epileptiform attacks. Nor does it include those occasions on which intravenous glucose was necessary in the afternoon or evening. The table refers exclusively to intravenous interruption necessary during the period of morning comas, and tabulates the reasons for its use.

In this table there is an apparent contradiction to what has been said before regarding the interruption of epileptiform convulsions, in that two patients (Cases 17 and 18) were interrupted intravenously when epileptiform fits threatened. Both these patients were adversely affected mentally by fits, and often vomited and refused food. Premedication by luminal was tried unsuccessfully in both cases.

In the course of 1937, two serious emergencies with danger to life occurred. The first was in a male aged 34 with a paranoid schizophrenic history of eleven years. He was of the thin asthenic type. There was also a history of previous cardiac collapses, and his treatment was undertaken with reluctance. Twenty-eight comas were given without serious incident, except that irregularity of the pulse was frequent, and was accompanied at times by cyanosis. The twenty-ninth coma was induced by 70

units, the same dose as on the preceding days. At 10.5 a.m. an epileptiform attack occurred, followed by an unusual pallor. The patient suddenly became pulseless, and his veins were so collapsed that intravenous glucose proved impossible. 0.5 c.c. adrenaline 1:1,000 was given subcutaneously, followed at once by 2 c.c. of 33½% glucose intracardially. Restoration was immediate, and intravenous glucose possible. There were no subsequent ill-effects, but in view of the chronic nature of the psychosis, cessation of the treatment was decided upon.

TABLE I.—REASONS FOR INTRAVENOUS INJECTION OF 33% GLUCOSE.

No. of case	Total insulin days	Failure to arouse 30 minutes after tube feed <i>a</i>	Epileptic attack after interruption by tube <i>b</i>	Introduction of nasal tube impossible	To avoid threatened epileptic fit.					Cardio-vascular reasons	Vomiting of feed
					Severe myoclonic twitchings	Laryngospasm					
1	64									1	
2	35	1								2	
3	56	3	1*								
4	44	2									
5	45										
6	71	10									
7	39	1	1								
8	94			1							
9	78	3								1	6
10	64				4						
11	82	2								1	
12	118	3									
13	26	1									
14	71	1									
15	79	11									
16	78										
17	92	8		1		10					
18	78	3		1		1					
19	72	7								1	
20	58	1									
21	67								1	1*	
22	61	1									
23	87	6								2	
24	69										
	1,628	64	2	8	4	11	5	5	12	106	

*a* = In this column patients were roused immediately with intravenous glucose, and showed hypoglycaemia.

*b* = In this column patients exhibited delayed awakening accompanied by hyperglycaemia. Emergencies marked \* are described in detail because of their severity.

We quote the second of our two dangerous emergencies in some detail on account of the lessons we believe can be learned from its consideration, and the wide fields of speculation it opens. It occurred in a male, a recent paranoid schizophrenic, aged 24. His physical condition was excellent, but no improvement in his mental state had taken place after 29 comas, and it was decided to extend gradually the length of coma. His thirtieth coma was induced by 130 units. He became unconscious at 9 a.m.; at 10.45 the corneal and plantar reflexes disappeared, and the patient was hypotonic. He was allowed to remain in this deep coma until 11.20, when interruption took place. No anxiety was felt about the patient, but at 11.50 he was not awake; restless motor movements, with opisthotonus, and flushed face, were noted. On examination the corneal reflexes were again present, but the plantar responses were both extensor. The pulse-rate rose to 140 and the blood-sugar was 230 mgm. per 100 c.c. at this time. This estimation was not known when 100 c.c. of glucose were given intravenously in the belief that the above symptoms were due to hypoglycaemia. No further glucose was given. This case emphasizes what is seen in Table I. If hypoglycaemia persists after the tube feed, awaking after intravenous glucose is certain and immediate.

The difficult cases are those in which coma persists in spite of hyperglycaemia (Freudenberg, 1937).

12.45 p.m. : No change ; 2 c.c. (1,000 units) of vitamin B<sub>1</sub> (Roche) and 8 c.c. calcium chloride solution (0.8 grm.) were given intravenously, the former for its effect on sugar utilization (Freudenberg, 1937), the latter to counteract the alkalosis known to exist in such conditions.

1.30 p.m. : Condition unchanged ; blood-sugar 235 mgm. per 100 c.c. 2 c.c. (1,000 units) of vitamin B<sub>1</sub> (Roche) given intramuscularly.

1.50 p.m. : Lumbar puncture carried out, and 15-20 c.c. of clear fluid under pressure removed. The sugar in the cerebrospinal fluid stood at 300 mgm. per 100 c.c., comparing very nearly with a similar case quoted by Molony and Honan (1937).

2.20 p.m. : Blood-sugar 180 mgm. per 100 c.c. Pulse 120.

2.40 p.m. : Semiconscious and answering vaguely. Perseveration present. Reflexes normal.

4 p.m. : Blood-sugar 100 mgm.%, pulse 108. Drank some tea.

5.30 p.m. : Temperature 101° F.

During the next three days the patient slowly improved, but vomiting, headache, and somnolence with restless intervals were present. On the fourth day he began to talk, and on the sixth day showed a return of insight and disappearance of paranoid ideas. He made an uninterrupted recovery and has resumed his work. Later experience outside the series under review has taught us that a blood transfusion would have been of the utmost value as an aid to restoration.

We learnt from this case that to prolong deep coma up to so long a period as one and a half hours may be followed by difficulty in restoring the patient. On the other hand the excellent therapeutic result obtained surely shows that prolonged deep coma may be necessary in certain cases, in spite of its added risk.

*Late hypoglycaemia.*—Among the 1,628 patient-insulin days, there were 18 occasions on which hypoglycaemic symptoms returned in the afternoon or evening. They were all due to insufficient meals, or vomiting during the day, and careful instruction of the nursing staff on the necessity for adequate meals has reduced such events to a minimum. They were dealt with by the introduction of glucose either by mouth, by tube, or intravenously.

#### CLASSIFICATION OF RESULTS

We urge the adoption of some standard method of classifying results. Our own series is classified strictly on the lines suggested by Müller (1936), which are as follows :—

(1) *Complete remission.*—This category represents complete disappearance of schizophrenic symptoms, with normal affective relationship, full insight, and ability to return to the normal sphere of work.

(2) *Incomplete remission.*—This category includes patients who are able to work but with persistence of any one of the psychic symptoms described under (1).

(3) *Partial remission.*—Patients in this category are able to resume work ; but symptoms remain without interfering with their daily life.

(4) *Unimproved*, and requiring hospital care.

It has seemed to us wise to classify our own results on Müller's categories, for the sake of comparing our figures with published Swiss results.

Experience of these categories has shown us many difficulties in accepting them entirely, difficulties that we believe are shared by other workers.

Table II summarizes our results.

TABLE II.

No.	Diagnosis	Results				Insulin days	Comas	Insulin fits	Cardiazol fits	Total dose (units)	Average daily dose	
		+++	++	+	0							
<i>Cases under 6 months</i>												
1	Catat.	+++				64	39	1	0	1,351	21.1	
2	Paran.	+++				85	21	0	0	3,025	84.4	
3	Paran.		++			56	30	1	3	5,980	106.7	
4	Paran.	+++				44	32	0	0	4,705	109.0	
5	Cat. stu.	+++				45	19	1	3	8,382	186.2	
<i>Cases from 6-12 months</i>												
6	Cat. stu.		++			71	53	0	3	6,185	87.0	
7	Cat. stu.		++			39	11	0	1	5,685	145.9	
<i>Cases from 12-18 months</i>												
8	Cat. stu.		++			94	7	1	9	10,200	108.5	
9	Paraphr.			0		78	63	0	0	6,047	77.5	
10	Catat.		++			64	24	1	0	7,495	117.0	
<i>Cases over 18 months</i>												
11	Cat. stu. (3 years)		++	*		82	59	0	5	17,395	212.0	
12	Catat. (7 "			+		118	45	0	0	15,674	192.9	
13	Paran. (12 "		++	*		26	15	3	0	1,570	60.4	
14	Paran. (5 "			0		71	55	0	8	9,720	197.9	
15	Paran. (2 "			0		79	47	2	0	10,050	127.0	
16	Paraphr. (2-3 "			0		78	37	24	0	10,910	198.5	
17	Hebeph. (3 "			0		92	41	5	0	11,460	124.5	
18	Cat. stu. (3 "			0		78	31	7	2	5,360	68.9	
19	Cat. stu. (7 "			0		72	39	0	4	6,435	89.3	
20	Cat. stu. (8 "			0		58	11	1	21	5,260	107.9	
21	Paran. (11 "			0		67	27	1	0	2,590	38.6	
22	Cat. stu. (12 "			0		61	33	2	23	7,015	115.0	
23	Hebeph. (2 "			0		87	57	1	0	4,855	55.9	
24	Hebeph. (2 "			0		69	42	22	0	4,806	69.6	
Totals		4	7	1	12	3	1,628	838	73	77	172,164	2521.6

+++ = Complete remission. ++ = Incomplete remission. + = Partial remission.  
0 = Unimproved. \* = Tendency to remission.

Cases improved with insulin and cardiazol fits are underlined.

The table demonstrates that out of a total of 10 cases (the total of the first three groups) with symptoms lasting up to eighteen months, nine have returned home and resumed their former occupations. Of the 14 long-standing cases treated, only three show remissions; two have returned home, the third awaits his discharge. It is of interest to note that these three older cases have previously shown a tendency to remission. Some of the old-standing cases treated showed clinical improvement.

Our longest period of treatment is one hundred and eighteen days, our shortest twenty-six days. The average, 67.8. The average total in-patient stay by each patient is about seventy-eight days, a remarkable figure when compared with the time spent in hospital by spontaneous remissions in recent cases, given as two hundred and two days by Dussik (1936). The patient who had treatment only twenty-six days made a rapid recovery, and after a fortnight's probation was allowed to return home, where she remains in very good health, managing a new house. The duration of treatment presents problems at times. Müller (1937) pointed out that insufficient length of treatment produced less satisfactory results. Therefore we have tried to follow his suggestion that at least sixty insulin-days elapse before treatment is abandoned as unlikely to be successful.

Comparing the two broad groups of cases shown in the table—up to eighteen months' duration and over eighteen months—there are several points of interest to be observed. It looks from the table as if the older cases used more insulin for the hypoglycaemic effects, but after calculating the average daily dose for each group we find that the average for the recent cases is 104.5 units, and that for the older group

105.6 units. Again, taking these two broad groups, we find that the percentage of insulin fits per hundred insulin-days is 1.67% in the recent group, and 6.54% in the old-standing group, a fact of interest in relation to the physiopathology of schizophrenia. These percentages closely correspond with the figures given by Plattner and Frölicher (1937).

#### RESULTS COLLECTED BY THE BRITISH PSYCHIATRIC INSULIN SOCIETY

By the kindness and courtesy of members of the British Psychiatric Insulin Society we are able to present a summary of a further 94 cases which, added to our own 24, make a grand total of 118, out of which number one patient died. The figures have been given to us by Dr. Finiefs, of the Three Counties Hospital; Dr. Hunter Gillies of the West Ham Hospital; Dr. Hamilton of the Bethlem Royal Hospital; Dr. Larkin of West Ham Hospital; Dr. Russell of St. Bernard's Hospital; Drs. Sieghem and Grace Watson, whose work has been done at Millbrook House.

To these generous colleagues and to their Superintendents we tender our grateful thanks. By their kindness we are enabled to give to this Section a table of results which would have taken any one of us alone some years to collect. Cardiazol combined with insulin has been used by most of our colleagues.

TABLE III.

Duration of symptoms	No. of cases	Complete and social remissions		Unimproved
		Cases	%	
Cases under 6 months ...	22	19	—	3
Cases from 6-12 months ...	18	15	—	3
Cases from 12-18 months ...	9	5	—	4
Cases over 18 months ...	69	22	—	47
Total	118	61	51.7	57

Average duration of insulin treatment = 61.4 days.

In Table III we have not adhered to Müller's categories, but summarize results in one column as "complete and social remissions", thus grouping together Müller's "complete, incomplete, and partial, remissions". Further, we do not think that the small numbers in each group of cases justify the use of percentages. We have therefore shown the total percentage only of all groups treated, from those of less than six months' duration up to those of long standing, even up to twelve years. The joint percentage of complete and social remissions works out at 51.7%, which may be compared with a table quoted by Müller (1937), and compiled from 381 Swiss cases treated for a sufficient period. His figure is 52.5%. It is worth noting that in this table of our united cases, in those groups in which the psychosis had lasted up to eighteen months, a total of 49, only 10 remained unimproved, or, put another way, 39 out of 49 recent cases are at home and working.

We submit that if generous allowances be made for differences in diagnosis and estimation of results, these figures are still ahead of spontaneous remissions (30-40%), and other methods of treatment. It remains to be seen how durable these remissions will prove.

#### SUMMARY AND CONCLUSIONS

We have surveyed briefly the experience gained in a year's insulin therapy at Moorcroft House; reference has been made to certain points of technique, and 24 completed cases have been reviewed.

There have been no fatalities, and but two serious emergencies in 1,628 patient insulin days. The combined use of cardiazol and insulin has been mentioned, but limited experience makes it impossible to decide whether insulin alone, cardiazol alone, or the combined methods will ultimately prove most effective.

Results, and details of interest, have been tabulated. The combined results of work at Moorcroft House and other hospitals have been collected and are appended, making a total of 118 completed cases with one fatality.

The clinical results in recent cases appear to be very satisfactory, and the great reduction of the period of residence in hospital cannot be overlooked.

#### REFERENCES

DUSSIK, K. T. (1936), *Rocznik Psychiat.*, **28**, 1936.  
DUSSIK, K. T., and SAKEL, M. (1936), *Ztschr. f. d. ges. Neurol. u. Psychiat.*, **155**, 851.  
FREUDENBERG, R. (1937), *Wien. klin. Wchnschr.*, No. 16, 5851.  
Id. (1937), *Schweiz. Arch. f. Neurol. u. Psychiat.*, **39** Ergn., 215.  
GEORGI, F. (1937), *Schweiz. Arch. f. Neurol. u. Psychiat.*, **39** Ergn., 49.  
JAMES, G. W. B., FREUDENBERG, R. and CANNON, A. T. (1937), *Lancet* (i), 1101.  
MOLONY, C. B., and HONAN, M. S. (1937), *J. Ment. Sc.*, **83**, 347, 680.  
MÜLLER, M. (1937), *Schweiz. Arch. f. Neurol. u. Psychiat.*, **39** Ergn., 17.  
PARFITT, D. N. (1937), *Proc. Roy. Soc. Med.*, **31**, No. 2, 137.  
PLATTNER, P., and FRÖHLICHER, E. (1937), *Ztschr. f. d. ges. Neurol. u. Psychiat.*, **160**, 785.  
SAKEL, M. (1935), "Neue Behandlungsmethode der Schizophrenie", Vienna.

## Section of Neurology

President—ANTHONY FEILING, M.D.

[January 20, 1938]

### DISCUSSION ON THE ROLE OF TRAUMA IN THE PATHOLOGY OF ORGANIC NERVOUS DISEASE (EXCLUDING EPILEPSY)

**Dr. Hugh G. Garland:** *Introduction.*—The subject chosen for discussion to-night is one of extreme difficulty and of the widest scope. Every patient is only too anxious to attribute his symptoms to some injury, serious or trivial, and there is probably no disease in which there is not a recorded example of a medical man sharing the opinion of his patient. From the extensive literature on the relationship between trauma and diseases of the nervous system one can find examples of every nervous disease and symptom-complex, and we are at once confronted with an important consideration—if trauma is an accepted aetiological factor in certain diseases must we assume that it may play a part in *all* nervous disease, or alternatively may such effects be limited to a small group of diseases? It is interesting to read the varying replies to this question from distinguished neurologists. In recent years Wilfred Harris (1933) and Pritchard (1934) have suggested that trauma must be seriously considered as a possible factor in many, if not all, nervous disorders. Kinnier Wilson (1923) could not accept trauma as a factor in any of the progressive nervous degenerations, or in cerebral tumour, though he was prepared to admit some possible association in disseminated sclerosis and neurosyphilis. On the other hand Collier and Adie (1926) made no reference to trauma in disseminated sclerosis though they felt that it might be a factor in tumour, and expressed contradictory views with regard to progressive muscular atrophy.

The varying and changing views of these English neurologists are representative of the general attitude throughout the world to this problem, but on the whole one can say that neurologists tend to minimize or deny completely any association. One cannot help feeling that one reason for this may be an inability to explain the possible mode of action of the injury.

If trauma may play some role in the aetiology of nervous diseases there are two important aspects of the problem, namely the purely scientific and the medico-legal, but in view of the usual absence of proof in the scientific sense we are largely limited to the medico-legal aspect.

It is a remarkable thing that in spite of the contradictory opinions expressed in medical literature there is never any difficulty in producing expert witnesses, in any case brought to the Courts, giving diametrically opposed views, neither party hesitating to give a dogmatic and final opinion. This has had a very unfortunate effect on the minds of the legal profession, and it would be of the greatest possible value if we could arrive at anything approaching unanimity in this discussion, even though we only agree to be uncertain.

I propose to limit my remarks even further than the title of the discussion suggests. Recent observations on the traumatic encephalopathy of the pugilist suggests that the results of multiple small traumata may be quite different from the results of the single injury. So far as I am aware there has been no striking incidence of disseminated sclerosis, neurosyphilis, or brain tumour in these cases, though at present the numbers may be too small to be of significance. Further, animal experiments, such as those of Vaubel (1932) in arthritis, have shown that pathological conditions can result from many small injuries, though not from a single injury, no matter how severe. We are perhaps not justified in drawing an arbitrary distinction between

single and multiple injuries, but I propose to limit myself to the possible effects of a single injury.

To turn to the methods of approach to this subject. I shall not discuss any of the conditions which are now regarded as being due entirely to trauma, or in which trauma certainly plays the most important role—for example such conditions as delayed ulnar palsy and chronic subdural haematoma. On looking through the literature one is rather surprised to see long discussions on trauma as the *cause* of a disease such as neurosyphilis or disseminated sclerosis. With regard to the former we are all agreed that infection is essential, and therefore the question of trauma as the *cause* does not arise ; at the same time there are factors other than spirochaetal infection which determine the production of neurosyphilis or one of its subdivisions. For example we know that there is often a relationship between habit of body and the development of G.P.I. or tabes, and everybody accepts these factors no matter how little we may know about their mode of action ; we cannot therefore dismiss other aetiological factors, including trauma, too lightly in certain cases. Similarly in disseminated sclerosis ; although the essential cause still eludes us surely nobody can subscribe to the view that in any one case trauma can be the sole cause.

I therefore propose to limit myself to those conditions in which we all more or less agree that trauma is at the most only one of several factors.

I cannot help feeling that the best possible approach to this subject would be a statistical one. A great deal has been written on the neurological syndromes found in large series of cases of war injuries, and most writers express the view that, owing to the infrequency of such conditions, we are entitled to say that trauma can therefore play no part. But unfortunately I can find no record of a control series of cases. We should like to know the incidence of disseminated sclerosis, for example, in a large series of uninjured males in the same age-groups, but this information does not seem to be available. It is also unfortunate that there is no material obtainable from civil sources. I have recently communicated with the Ministry of Pensions, but they could supply no information ; several insurance companies, who deal largely with the injured workman, were also unable to give me figures of any kind, and the most I could get was a statement that "such cases are uncommon". The insurance companies might render a great service both to themselves and to us if they would keep records of a large series of injuries with regard to the later development of organic disease.

Even the recorded experience of private practice is unreliable. Most cases of serious organic disease come sooner or later to the notice of a neurologist, but he probably sees every case in which a claim for compensation arises ; many of these are recorded in the literature, which therefore contains figures which are usually not, strictly speaking, unselected. There can be no doubt that the compensation factor complicates the issue very considerably ; it is only natural that the injured party should make the most of his injuries, and there can be little doubt that in many cases the history of the illness is deliberately modified to suit the compensation case. One can say therefore that at present there is really no statistical material of any value.

Pathological proof is equally disappointing, as most of the conditions under consideration are chronic, and even if histological examination becomes possible, the findings are the same as in cases in which there has been no injury. Unfortunately most of the diseases under consideration cannot be produced in experimental animals.

A comparison with non-neurological diseases is, again, of little value ; the recorded opinions of accepted authorities, on the role of trauma in such conditions as osteomyelitis or pulmonary tuberculosis, show that there is just as much difficulty as there is in our own problems.

It seems, therefore, that we must fall back on a few carefully considered and recorded experiences. In any given case we have three possibilities to consider. Firstly, that trauma plays no part. Secondly, that trauma has been the precipitating factor ; here we usually assume that the disease was present before the injury, in

an asymptomatic form, that it has in some way been stirred up by the injury and that it would subsequently have appeared even though there had been no injury (though this surmise is of no significance in law). Thirdly, that trauma has accelerated the progress of the disease or increased the severity of symptoms admitted to be present before the accident.

We have next to consider features of the trauma itself. While many neurologists are prepared to admit that injuries to the brain or cord may play a part in the production of central nervous disease, there are many who are unable to accept peripheral injury in the same light. The severity of the injury must be of considerable importance, but not only is severity very difficult to define, but many of the recorded cases are extremely vague on the point. Then there is the important question of the latent period. Here, I think, we have examples of some of the most contradictory and sometimes unjustifiable statements. For example, Wilfred Harris (1933) records disseminated sclerosis developing eleven years after a severe head injury, but Kinnier Wilson (1923) will not accept trauma as a factor in neurosyphilis unless symptoms arise or increase within forty-eight hours. The Americans attach great importance to "bridging symptoms" in this connexion, and many of them will only accept a traumatic factor in the presence of continuous symptoms between the injury and the finding of the objective changes of disease. Here again I feel that there can be no definite rule to be applied to all forms of organic nervous disease.

Before turning to a few of the common conditions for discussion I may say that I do not propose to review in any way the vast literature or even to burden it with a series of personal experiences.

*Disseminated sclerosis.*—Perhaps the commonest disease under discussion is disseminated sclerosis and in many ways it provides the most difficult problem, owing to its natural exacerbations and remissions. Again, I cannot accept trauma as being the *cause* of disseminated sclerosis, but I have been convinced from my own experience that it plays an *aetiological* role in some cases.

I believe that this disease is sometimes brought to light, or its symptoms increased, by a variety of external conditions. I have frequently seen symptoms appear during pregnancy—and, particularly, after parturition—and have seen several patients who have had no symptoms previous to delivery and have yet had widespread manifestations of disseminated sclerosis on getting up some two or three weeks later. I have seen exactly the same thing following minor operations, suggesting very strongly that peripheral trauma must be considered as a precipitating factor. I also hold the view, which I know is shared by several people here, that such things as anaesthetics, manipulations, lumbar puncture, and even some of the more spectacular forms of so-called "treatment" will increase the disability of disseminated sclerosis. It is a not uncommon story that the patient "was never quite the same" after lumbar puncture; here at least the compensation factor does not complicate the issue and, further, I do not think the same complaint is made in other organic nervous diseases.

Kinnier Wilson (1923) was prepared to admit that this disease can be precipitated by injury, even by peripheral injury; Collier and Adie (1926) made no reference to such an association, and Russell Brain (1929), in a critical review, was non-committal. On the other hand Wilfred Harris (1933) has recorded a series of cases in which, in his opinion, trauma played an important aetiological role; these formed 7% of his cases seen in private practice and included cases of cerebral, spinal, and peripheral trauma. In my own experience I have been rather impressed by the presence of "bridging symptoms" in these cases and have only seen the disease appearing after a long latent period in compensation cases. I should, however, like to mention one personal case in which bridging symptoms were absent but which is still very impressive:—

This was in a miner who sustained a severe injury to the back, without fracture, from a fall of roof. There were no immediate symptoms but three weeks later he began to drag his

left leg and from that time he has developed typical, slowly progressive, disseminated sclerosis. The right leg was not affected until two years afterwards, nor the arms for fourteen years, but he was bedridden within four years of the accident. The most careful inquiry has failed to elicit any suspicious symptoms prior to the accident and in spite of the absence of bridging symptoms during the latent period of three weeks I feel that in this case a severe injury to the spine was the precipitating factor.

*Neurosypilis.*—The literature relating to trauma and neurosyphilis is largely centred round tabes dorsalis and G.P.I. There are more references in the literature to the traumatic acceleration of G.P.I. than to that of other forms of neurosyphilis and, especially in the older literature, a traumatic factor was accepted in anything up to 5% of cases. The injury is almost invariably to the head. I have seen few cases in which trauma appeared to accelerate or precipitate tabes and only one case in which it accelerated G.P.I. Charcot's arthropathy sometimes develops after local injury, but this is, perhaps, a different problem. One is rather impressed by the absence of any increase of symptoms following peripheral trauma in tabes, which is unlike disseminated sclerosis in this respect. Many tabetics undergo abdominal operations, but I have never seen one such case in which the nervous condition was made worse. Further, although neurosyphilis is at least as common as disseminated sclerosis, there are far more recorded cases of the latter disease in which trauma was thought to be a factor.

At the same time it is well known that peripheral trauma may determine the development of cutaneous and other gummata at the site of the injury and I think we must admit the possibility of central nervous injury having a similar effect. There are several recorded cases of cerebral gumma following head injury, but this must be a very uncommon condition, and the accuracy of the diagnosis cannot usually be proved. There is the further difficulty with regard to the latent period in neurosyphilis; one has difficulty in believing that objective signs, such as pupillary changes and areflexia, can develop in this disease in the course of a few days.

Finally, therefore, I feel that, although central trauma may be of some importance, we should be very guarded in accepting peripheral trauma in the aetiology of neurosyphilis.

*Cerebral tumour.*—In considering the relationship between trauma and the subsequent development of brain tumour, reference must be made to the relationship of trauma to tumours in general. There can be no doubt that more work has been done, and more observations have been made, on this subject than on any other relating to trauma and disease. Most cancer research workers have increasing difficulty in convincing themselves that trauma plays any part whatever in the production of a tumour, and in a recent American review (Brahdy and Kahn, 1937) on this subject the concluding paragraph says: "It has become more and more clear that there is no reasonable evidence of any relationship between the single injury and the production of a cancer." On the other hand neurologists have always been impressed by the frequency of a history of head injury in tumour cases. Statistics have so far been unconvincing and have even confused the issue, as Parker and Kernohan (1931) found, in a series of 431 cases of glioma, a history of injury in 13.4%, though there only appeared to be a possible relationship in 4.8%; but in 431 patients suffering from various diseases 10.4% had had a head injury, and in a series of 200 normal persons the incidence of injury was 35.5%. If one can draw any conclusion from these figures, it is to the effect that trauma protects the individual from the subsequent development of a tumour—a conclusion which seems, to say the least, improbable.

Some authors demand that the tumour should develop at the site of the injury, but in view of the frequency of contre-coup damage one has difficulty in accepting this. Others demand a minimum latent period of six weeks and a maximum of two years, but owing to our ignorance as to the rapidity of growth in the early stages such arbitrary figures are difficult to accept.

Again we have to consider the histology of the tumour ; if one is satisfied that a meningioma may be determined by trauma it does not necessarily follow that this can also be applied to the glioma group. I have had one case of interest, in which a superficial glioma developed in the parietal region exactly beneath a scar on the scalp, the result of a head injury two and a half years prior to the onset of symptoms ; this tumour was very small but was considered by Dr. J. G. Greenfield to be a malignant type of glioma. This case seems suggestive, yet the latent period would be too long for the suggestion to be acceptable by many authorities, and there was a complete absence of bridging symptoms.

*Progressive muscular atrophy.*—Perhaps the most striking feature of the literature on this disorder is the complete reversal of opinion expressed by Collier and Adie between 1926, when they considered trauma to be an important factor, and 1929, when they decided that trauma played no part. Kinnier Wilson (1923) subscribed to the latter view and decided that trauma was not a factor in producing any of the progressive degenerations. On the other hand there are many observers who feel that trauma may precipitate this disease, and many who share the original view of Collier and Adie (1926) that even peripheral trauma may be sufficient and that wasting may commence at the site of the injury. As in the case of some other diseases under discussion, there is sometimes a difficulty as to whether the disease in question is really progressive muscular atrophy—whatever that may be. This difficulty has been emphasized in a recent paper by Walshe and Ross (1936) in which they describe a syndrome, in some ways resembling progressive muscular atrophy, following injury to the cervical cord. I have had a personal experience which is not only of interest in this connexion but may throw light on some other aspects of our discussion. In May 1936 I received a double injury to the skull and cervical region ; the area of trauma was clearly defined by subsequent bruising and tenderness. There was loss of consciousness for a few moments and on recovering I had complete paralysis of the arms, with intense paraesthesiae, from shoulders to finger-tips ; these disappeared within a few seconds and there were no immediate sequelæ, but in the following November the same intense paraesthesiae suddenly developed on flexion of the head. This sign is well known to neurologists and is seen after cervical cord injuries and in disseminated sclerosis ; it occurred in several of the cervical injuries recorded by Walshe and Ross (1936).

In my own case the symptoms slowly disappeared during the course of a few weeks. I have not developed any manifestations of disseminated sclerosis or of any other central nervous disease and am quite convinced that these symptoms were a result of the previous trauma, but the really important feature was the presence of the long latent period ; it seems probable that some small lesion developed in the cervical cord, though it produced no symptoms for five months.

I have at present under my care a man who sustained a severe injury in the cervical region, which has left some changes in the vertebrae as shown by X-rays, and who is suffering from a condition which is similar to that described by Walshe and Ross (1936) but, after three years, appears to be progressive. In spite, therefore, of many statements to the contrary, I cannot help feeling that trauma, at any rate to the cord, may produce organic changes, which may be delayed and even progressive and may possibly be true examples of progressive muscular atrophy.

*Paralysis agitans.*—The Parkinsonian syndrome is associated with several distinct pathological processes, and in its relation to trauma is comparable with progressive muscular atrophy. It seems clear that in some of the recorded cases the condition has really been a non-progressive syndrome probably due entirely to trauma, and therefore not strictly within the range of our subject. Most writers admit that debilitating and other influences may be exciting causes of this condition and Collier and Adie (1926) even stress the frequency of trauma, though here trauma is rather ill-defined as regards site and severity. There have been several recent examples of Parkinsonian syndromes following trivial peripheral injuries ; here I find some

difficulty in accepting the story, and I have had no personal cases of this kind. We know that damage to the peripheral nerves may be followed by changes in the related central nerve-cells, but in the case of Parkinsonism we should have to assume further ascending degeneration in a second series of neurones. It is a common experience that considerable increase of tone may exist in the limbs in these cases, even though no complaint may be made, and I feel that, especially in Parkinsonism, the peripheral injury may draw the attention of the patient to his disability rather than act as an aetiological factor. I feel therefore that perhaps we should make a distinction between peripheral and central injuries in this group of cases, and we must assure ourselves that a Parkinsonian syndrome following head injury is a true example of paraparesis agitans.

*Conclusion.*—I think that neurologists in the past have been too much inclined to dismiss trauma as being of any aetiological significance in nervous diseases. My own feeling is that although there is no proof in the scientific sense, there are many cases which seem to exceed the bounds of coincidence, and I feel that this applies especially to disseminated sclerosis.

#### REFERENCES

BRAHBY, L. and KAHN, S. (1937), "Trauma and disease", London.  
 BRAIN, W. R. (1929), *Quart. J. Med.*, **23**, 343.  
 COLLIER, J. S., and ADIE, W. J. (1926), Price's "Text book of the practice of medicine", London.  
 HARRIS, W. (1938), *Brit. M. J.*, **2**, 955.  
 PARKER, H. L., and KERNOHAN, J. W. (1931), *J.A.M.A.*, **97**, 535.  
 PRITCHARD, B. (1934), *Lancet* (ii), 945.  
 VAUBEL, E. (1932), *Beitr. z. path. Anat. u. z. allg. Path.*, **89**, 374.  
 WALSH, F. M. R., and ROSS, J. (1936), *Brain*, **59**, 277.  
 WILSON, S. A. K. (1923), *J.A.M.A.*, **81**, 2173.

**Dr. C. M. Hinds Howell:** This subject is of great theoretical interest, as well as of practical importance in its medico-legal aspects. Epilepsy has been specifically excluded from the discussion, and I take it that immediate and evident injury to the brain or cord, whether mechanical or infective, is also excluded.

When trauma is followed by signs of organic disease in the nervous system, there are three possible explanations for such an occurrence.

- (1) That the trauma was the essential cause of the disease.
- (2) That it rendered manifest symptoms and signs of an existing organic disease.
- (3) That the relationship between the injury and the appearance of organic disease was a pure matter of chance.

From the nature of the case absolute proof of the traumatic origin of organic disease cannot be established. In order to establish presumptive evidence of the relation of trauma to the subsequent disease certain desiderata would have to be satisfied.

- (1) The trauma must be of a serious character.
- (2) The subsequent development of organic disease must occur within a not-too-remote period.
- (3) The particular type of organic disease must be shown to follow injury sufficiently often to justify the presumption that the injury was a direct or indirect cause of its development.

The third point is the easiest to establish, because the first two raise questions in themselves which are difficult to answer, for instance as to what constitutes a serious injury. It is obvious that a trivial injury is unacceptable as a possible cause of organic disease. In the second place, can one say that there should be a definite time limit between the date of injury and the first symptoms of organic disease?

I would mention certain organic diseases in which trauma has been suspected of playing an active aetiological part. In connexion with the meninges: Arachnoiditis, and possibly tumour formation, also syphilitic meningitis; in the brain: G.P.I., paraparesis agitans, tumour; in the cord: Amyotrophic, and other less specifically

defined progressive degenerations, tabes dorsalis, and, throughout the central nervous system, disseminated sclerosis.

With regard to the syphilitic diseases—G.P.I., tabes, gummatous meningitis—it is of course clear that the trauma can only act as a precipitating factor, and I should think that its role in this connexion is generally recognized. I have seen it occur in several personal cases. Arachnoiditis is also generally believed to follow trauma in a definite proportion of cases.

The role of trauma in other members of the group that I have mentioned is less clearly established.

It is difficult, *a priori*, to see how trauma is likely to produce conditions differing so widely in their pathology as amyotrophy, disseminated sclerosis, and brain tumour, but we must bear in mind that we are at present quite ignorant of what actually causes these conditions—hence trauma cannot be excluded on *a priori* grounds.

So many cases have been reported of severe injury resulting in spinal concussion with some immediate paralysis, followed at a later date by a progressive deterioration, that the conclusion is unavoidable that the original trauma was the starting-point of the disease. How it acts is another matter and at present entirely speculative.

Wilfred Harris (*B.M.J.*, 1933 (i), 915) reported a number of such cases in his Saville Oration in 1933. In a number of these the patient subsequently developed symptoms typical of disseminated sclerosis. I do not think all his cases could be accepted as evidence of a causal connexion between trauma and disseminated sclerosis. In one case, for instance, a boy aged, I think, 15, had a severe trauma from which he recovered, played racquets for his school, and two and a half years later developed symptoms of disseminated sclerosis. I should regard a period of this length as being too long to show a causal relationship of the trauma to be accepted. But the cases he quotes are in most instances much more convincing than this one, and certainly merit careful consideration. Until we know more about the aetiology of disseminated sclerosis I, personally, am not prepared to admit that trauma is a factor in the production of such a specialized type of disease, from the pathological point of view, as is disseminated sclerosis.

It is a different matter, I think, with regard to chronic degenerative diseases, such as amyotrophic lateral sclerosis and paralysis agitans. I can well imagine shock from concussion initiating a condition of abiotrophy from which the nerve-cells never recovered, but this sequel is very rare. Thousands of men suffered from severe spinal concussion and spinal and cerebral trauma in the late war, but I do not think that this was followed by any considerable increase in the number of cases of amyotrophic lateral sclerosis, paralysis agitans, or disseminated sclerosis.

I suppose we have all seen cases of amyotrophic lateral sclerosis or paralysis agitans in which the first-known symptoms occurred within a few weeks of serious injury. I was taught by our dear friend, the late James Collier, that trauma was an outstanding cause of amyotrophic lateral sclerosis. Collier wrote this in the 1926 edition of a well-known textbook. He said that this conclusion was reached as the result of analysis of a surprisingly large number of cases at the National Hospital. Three years later he calmly announced in the same textbook that the evidence for trauma being a factor in the production of amyotrophic lateral sclerosis was quite unsatisfactory.

I have seen several cases of this disease and of paralysis agitans, in which the conclusion seemed unavoidable that trauma had been the starting-point of the disease. Grimberg, however, in a paper published in the *Journal of Nervous and Mental Diseases*, 79, 14-42, analyses 86 cases of so-called traumatic paralysis agitans and concludes, rather dogmatically, I think, that trauma cannot cause this condition.

If trauma is ever a cause of brain tumour it must be a very rare one. I do not know of any evidence to show that brain tumour developed in any considerable number of the cases of head injury in the Great War. It is difficult to know what

evidence would be acceptable as showing that injury to the head was the cause of a brain tumour. It would, I think, have to be found growing at the site of the scar, either in the meninges or cerebral tissue.

The conclusion I have reached is that trauma may be the starting-point of certain degenerative conditions in the brain or cord, but is more frequently a precipitating factor in the appearance of organic disease.

**Dr. S. P. Meadows** said that he had recently examined the records of cases of disseminated sclerosis seen personally, and of 140 such cases there were only five in which the first appearance of symptoms had followed shortly after an injury. In one further case the patient, already the subject of disseminated sclerosis, had developed new symptoms in an upper limb shortly after an injury to the wrist.

Dr. Russell Brain had also examined the records of his own cases, and in three out of 81 cases there was a history of injury to one limb, shortly before the onset of symptoms in the injured limb. Thus, out of a total of 221 cases of disseminated sclerosis, in only 4% could trauma be considered as a possible aetiological factor. In six of these nine cases, injury to one limb had been followed by weakness or paraesthesiae affecting that limb. In only one case had there been a head injury, and this had not been severe.

He (the speaker) had had one case of developed disseminated sclerosis, in which the patient was severely injured. His right arm was almost severed below the elbow, and the left radius and ulna were fractured, but the injury had no effect on the course of the disseminated sclerosis, which was slowly progressive.

---

**Dr. Wilfred Harris** : For many years I have been impressed by the importance of trauma in the history of the development both of progressive muscular atrophy and—especially—of disseminated sclerosis. [Dr. Harris gave details of several cases of disseminated sclerosis in which the disease had followed directly upon the injury.] In my opinion, seeing that we have no real knowledge whatever of the pathology of either of these diseases, we have no right to assume that trauma has no influence either in the aetiology or in the development of the disease, for the simple reason that we do not understand how it would act.

**Dr. Denny-Brown** said it appeared to him that the greatest difficulty in allocating a contributory role to trauma in the precipitation of progressive generalized nervous diseases, such as disseminated sclerosis and nervous syphilis, was the establishment of the pathological process occurring in the latent interval.

It had been striking, in his experience of a few such cases, that there had been an emotional disturbance following the injury, sometimes mild, and sometimes severe. If the disturbances were mild it might be referred to by the patient as only that he had been "badly shaken" by his injury. Close inquiry would elicit that the disorder to which the patient referred was an emotional lability with insomnia and some degree of depression, such as was commonly experienced for an interval after sudden fright, whether an actual injury occurred or was just avoided. Such emotional disturbances, even though mild, are commonly accompanied by a constitutional upset, characterized by some loss of weight. Though it was difficult to establish that this occurred in patients who subsequently developed a nervous disease, it appeared reasonable to him that this constitutional disturbance was the factor which provided an explanation for the sudden onset of a generalized disease within a short and apparently symptomless interval from trauma.

A further difficulty was the explanation of the slight incidence of such generalized disease following severe injuries, as in a war, compared with the effect of relatively minor injuries. The more severe injury entailed a period of rest in bed, and this perhaps minimized the effect of the constitutional disturbance on the nervous system.

## Section of Urology

President—HENRY WADE, C.M.G., F.R.C.S.

[January 27, 1938]

### Renal Calculi, Renal Disease, and Hyperparathyroidism

By FRANK SCOTT FOWWEATHER, M.Sc., M.D., Ch.B., D.P.H.,  
M.R.C.P., and LESLIE N. PYRAH, M.Sc., Ch.M., F.R.C.S.

(From the Department of Pathology and Bacteriology, and the Department of Surgery,  
University of Leeds)

THE association of renal calculi with hyperparathyroidism is now well recognized. Albright, Baird, Cope and Bloomberg (1934) give many references to published cases in which this association is evident, and found that renal calculi were present in 23 out of a total of 83 cases of hyperparathyroidism, i.e. an incidence of 27%. They consider that the presence of renal calculi should always arouse a suspicion of an underlying hyperparathyroidism.

These authors consider that the kidney may be involved in hyperparathyroidism in three different ways, which they refer to as Types I, II, and III. In Type I, as a result of the increased urinary excretion of calcium and phosphorus, calcium phosphate is precipitated in the renal pelvis, and in the subsequent course of the disease there are recurring renal stones. Type III is, in effect, an acute parathyroid poisoning, with calcium deposits in many organs besides the kidneys. It is the condition seen in dogs after excessive doses of parathormone; and a naturally occurring human case believed to be of this type is described. In Type II it is considered that calcium phosphate is precipitated in the renal tubules, forming concretions in the kidneys which eventually lead to inflammatory changes, sclerosis, and contracted kidneys. They suggest the term "chronic parathyroid nephritis" for the kidney lesions in this group, though, in view of the fact that the initial disturbance is not inflammatory, they consider the term "chronic nephrocalcinosis" to be preferable.

Albright *et al.*, therefore, consider that where hyperparathyroidism and renal disease exist together, the latter is, in general, the result of the former. They do, however, point out the possibility of the reverse being the case. "This would only have to be considered in the few cases where multiple parathyroid glands were involved. Since the parathyroid hormone raises blood-calcium and lowers blood-phosphorus, any influence opposing these actions might be attended by hyperplasia of the glands. It seems conceivable, therefore, that a chronic renal insufficiency with phosphatic retention and a high inorganic phosphorus level might likewise cause hyperplasia of all parathyroid tissue which might go on to multiple tumour formation. As far as the writer is aware, of all the cases with hyperparathyroidism, only those with kidney damage have shown multiple tumours. In these cases, the kidney damage may be the cause and not the result of the parathyroid tumours."

Castleman and Mallory (1935) have made a study of the parathyroid glands in hyperparathyroidism, and as a result they divided these cases into two groups. One group—the smaller one—was characterized by a diffuse uniform alteration of all the parathyroid tissue of the body. In the second group one gland (often only a part of it) was abnormal—rarely parts of two glands were abnormal—whereas the remaining parathyroid tissue was grossly and microscopically within the limits of normal variation. They consider that the first group is to be regarded as hyperplastic, dependent on "some chemical, hormonal, or nervous stimulation", while the second group falls within the accepted limits of neoplasia.

These authors studied 160 cases of probable hyperparathyroidism taken from the literature, together with 25 cases of their own. Of this total of 185 cases, 146 showed single gland enlargement and 39 showed multiple gland enlargement. So far as the incidence of bone lesions and renal calculi is concerned, Castleman and Mallory give the following figures :—

	Present series (Castleman and Mallory)		Cases in literature	
	No.	% of total	No.	% of total
Osteitis fibrosa alone	5	20	70	59.8
Renal stones alone	11	44	3	2.52
Osteitis fibrosa plus stone	9	36	46	38.6

The difference between these two sets of figures they believe to be due to the fact that the association of renal stones with hyperparathyroidism was rarely recognized by the earlier writers on the latter subject. In the cases where renal stones alone are present, the criteria for the presence of hyperparathyroidism also is taken by these authors to be a high blood-calcium and reduced blood-phosphorus. The same criteria seem to have been adopted by Albright *et al.*

Of Castleman and Mallory's own cases, five out of six believed to show parathyroid hyperplasia came in the group of renal stones without bone changes—only one showed significant bone lesions. This, however, they believe to be the result of chance sampling since nearly all the cases of hyperplasia collected from the literature showed bone lesions. Hence they conclude "either type of hyperparathyroidism may be associated with stone formation only, bone changes only, or the combination. As a rule the stone formation comes first and bone lesions follow only after a period of years".

Certain other workers have looked at the problem from the opposite direction, i.e. instead of studying the presence of renal disease in hyperparathyroidism, they have studied the evidence for hyperparathyroidism in renal disease. Pappenheimer and Wilens (1935) quote the work of Bergstrand who, in a routine study of the parathyroids in 200 autopsies, found a small percentage in which the glands were "distinctly enlarged" and in most of these cases there were, at the same time, more or less severe changes in the kidneys. Subsequently, a series of nephritic cases were studied; in 10 of 50 cases the combined parathyroid weights exceeded 200 mgm., which he regards as the upper limits of normal. This and other work, suggesting as it does a relation between renal disease and parathyroid enlargement, caused Pappenheimer and Wilens to begin a systematic study to determine whether disease of the kidneys might not lead quite regularly to enlargement of the parathyroids. For this purpose they dissected out the parathyroid glands in a series of nephritic and control cases, and weighed each gland separately. They found that the mean weight of the parathyroids in various types of chronic renal disease exceeds that of non-nephritic cases. In an unselected series this increase in mean weight is approximately 50%; in cases with advanced renal lesions the increase amounts to more than 100%. The increase in weight of the parathyroids is roughly proportional to the severity and extent of the renal lesions and to the intensity of the clinical signs of renal insufficiency. Usually three or four of the glands share in the enlargement. It is of interest to note that the group of cases in which renal lesions were found at autopsy but in which symptoms of renal inefficiency were not recognized, nevertheless showed in most cases a certain degree of parathyroid enlargement. In the recent careful study of the weight of the parathyroid glands by Gilmour and Martin (1937), attention was also directed to the condition of the glands in renal disease. They divided their renal cases into two groups, viz. toxic nephritis (Russell, 1929), and renal disease of other types. They found these two renal groups to contain relatively numerous examples of unusually large glands showing histological evidence of abnormal activity.

Our own interest in this subject was first aroused by the work of Castleman and Mallory, and particularly those aspects of it which appeared to have an important bearing on the question of the treatment of renal calculus. The argument regarding treatment, dependent on Castleman and Mallory's findings, appears to be as follows:—

If hyperparathyroidism is a significant cause of renal calculus and if the appearance of calculi is likely to be followed later by the bone lesions of osteitis fibrosa, then the removal of the hyperparathyroidism should be the principal aim in treatment, for by that means not only would recurrent calculus be prevented but the patient would also be spared the late development of osteitis fibrosa. In cases of hyperparathyroidism dependent on hyperplasia, resulting from some external stimulus, removal of enlarged parathyroids would probably not be of permanent value as the hyperplasia would be likely to recur (p. 46), but in cases of neoplasia removal of the tumours might be expected to effect a permanent cure. Since either type of hyperparathyroidism may be associated with stone formation only (p. 41), and since the localized tumour type is far more common than generalized hyperplasia (p. 44), parathyroid tumours should be found in a large proportion of cases of renal calculus with evidence of hyperparathyroidism. Moreover it is claimed (p. 41) that the diagnosis of hyperplasia should be possible, as a rule, from the histological examination of a single gland, even from a frozen section during operation.

The logical course to pursue, therefore, would be to seek for evidence of hyperparathyroidism, i.e. raised blood-calcium (and reduced blood-phosphorus) in all cases of renal calculi, and where this is positive, to make a search for parathyroid tumours. If such are not readily found a biopsy should be made of any parathyroid tissue available, and, if the presence of hyperplasia is not shown, a further search should be carried out until tumours are found and removed.

With this argument in mind we commenced an investigation of cases of renal calculus, particularly those with recurrence, to find out which of them showed evidence of hyperparathyroidism, and for which, therefore, the above principles of treatment might have to be considered. Soon, however, the evidence of hyperparathyroidism associated with various types of renal disease came to our notice. Renal calculi, particularly if of long standing or recurrent, are frequently the cause of damage to the kidneys. Hence, on this evidence, hyperparathyroidism associated with renal calculi might not be the cause of the calculi but the result of renal damage caused by them and the principles of treatment already outlined above could not be applied. With a view to obtaining further information on the whole subject we therefore extended our investigation to include blood-calcium determinations on other surgical cases involving the kidneys and on cases of renal disease in the medical wards. The presentation of the results of this investigation and their bearing on the problem outlined above is the subject of the present paper.

Since the blood-calcium concentration is the principal figure which will be considered, it is important to decide what value is to be taken as normal. The normal range for blood-calcium given by most textbooks is 9-11 mgm. per 100 c.c. of serum (or plasma). We thought it would be of interest to find out how far our own figures agreed with this range. Accordingly we have examined all blood-calcium determinations made in this laboratory during the two years preceding the commencement of this investigation. The determinations have been made on patients of the Leeds General Infirmary, at the request of members of the clinical staff, in the course of the ordinary clinical investigation of these patients. The result of our examination is as follows:—

Total determinations—169

Cases showing figures from 9-11 mgm. . . . .	103
Cases showing figures over 11 mgm. . . . .	52
Cases showing figures under 9 mgm. . . . .	14

In the consideration of hyperparathyroidism it is only the upper normal limit which is of importance ; hence the cases showing values below 9 mgm. need not here be further considered. In the cases where figures of over 11 mgm. were found, the clinical records were carefully examined, and as a result we arrived at the following classification :—

(a) Cases with bone disease	..	..	..	..	32
(b) Cases having treatment likely to raise the blood-calcium	..	..	..	..	7
(c) Cases with recognized or suspected renal disease	..	..	..	..	7
(d) Other cases	..	..	..	..	6

It will be shown subsequently that a significant proportion of cases with renal disease have a raised blood-calcium. Hence, only the six cases under (d) cannot be considered as the result of some condition known to be capable of causing a raised blood-calcium concentration. Of these, three gave values of 11.1 mgm., one of 11.2 mgm., one of 11.4 mgm., and one of 11.5 mgm. When one compares this number with the number of cases giving values between 9 and 11 mgm., viz. 103, it will be realized that the number of cases without some known condition tending to raise the blood-calcium, which give values exceeding 11 mgm., is relatively small. In other words, while normal cases may occasionally be met with which give values exceeding 11 mgm., their number is so small that where the value significantly exceeds this figure the case should be regarded with suspicion, and not accepted as normal until known causes of disturbance of blood-calcium have been excluded.

The number of cases in which we had previously made determinations of the blood inorganic phosphorus was not so great as those in which we had made blood-calcium determinations, and hardly seemed sufficient to justify treatment in the same way ; figures collected from the literature by Peters and van Slyke (1931) indicate a normal range for adults of 2-5 mgm. per 100 c.c. serum and for infants, 4-7 mgm. In our own experience the majority of figures from normal adults lie between 3 and 4 mgm., while normal children have given values, mostly in the neighbourhood of 5 mgm., and young infants 5.5-6 mgm.

The normal phosphatase of blood depends on the method used ; the figures given in the paper have all been obtained by the method of Jenner and Kay (1932), for which 10 units is the upper normal limit in the great majority of cases.

The normal maximum blood urea-nitrogen, as given in a summary by McKay and McKay (1927) is 23 mgm. From our own experience of hospital patients, and by the method in routine use here, we prefer a somewhat higher maximum, viz. 25 mgm.

The cases we have dealt with fall into three main groups :—

- I.—Cases with renal calculi.
- II.—Cases with enlarged prostate.
- III.—Cases with renal disease in the medical wards.

*Group I.*—Cases which had previously undergone treatment here for renal calculi were asked to come up for re-examination. Evidence of recurrence was looked for, and blood-calcium estimations were made. In most cases where the blood-calcium was found to exceed 11 mgm. determinations of blood-phosphorus and phosphatase were also made. Table IA contains the data relating to patients in whom recurrence was found or in whom recurrence was known to have occurred previously. Table IB contains cases with no evidence of recurrence, and Table IC, cases in which evidence of recurrence is not conclusive.

During the course of the investigation other cases of renal calculi that came under our notice were included within its scope ; these are included in Table ID. Inquiry into the history of these cases showed that some of them were suffering from a definite recurrence of stones, while in others the history was entirely negative from this point of view. Three other cases without definite evidence of calculi are included in Table IE.

TABLE IA.—RECURRENT CALCULI.

No.	Sex	Age	Operation and year	Previous findings			Present findings			
				Blood urea-nitrogen	Urine	Culture	Clinical and X-ray	Blood-calcium	Blood-phosphorus	Blood-phosphatase
1	M.	59	Pyelolithotomy (1928) (R.)	25.5	—	Staph.	Several calculi in rt. kidney	12.6	1.9	4.8
2	M.	38	Nephrolithotomy for recurrence of renal calculi (1936)	36.6	—		X-ray—no calculus	12.0	2.4	1.9
3	M.	33	Pyelolithotomy (1929) (L.)	28.8 (1929)	No pus		? calculus	11.6	3.0	4.8
4	M.	64	Pyelolithotomy (1929) (L.)	—	Pus		Hematuria. X-ray shows stone left lowest calyx	11.5	2.2	5.8
5	F.	49	Pyelolithotomy (1925) (R.)	15.5	No growth		Much dragging pain rt. loin. Small calculus (R.)	11.4	3.4	3.8
6	F.	28	Pyelolithotomy (1931) (L.)	24.8	No growth		X-ray—definite recurrent stone (L.)	11.3	2.4	5.1
7	M.	—	Pyelolithotomy (1929) (R.)	25.6	Sterile		X-ray—large calculi both kidneys	10.8	—	—
8	M.	—	Nephrolithotomy (1928) (R.)	24.6	—		X-ray—multiple calculi (R.) ? tiny shadow (L.)	10.7	—	—
9	M.	—	Pyelolithotomy (1926) (R.)	20.9	Pus		X-ray—large recurrent stone (R.)	10.7	—	—
10	F.	—	Pyelolithotomy (1924) (R.)	—	Pus and R.B.C.s		X-ray—small recurrent stone lowest calyx	10.5	—	—

TABLE IB.—NON-RECURRENT CALCULI.

No.	Sex	Age	Operation and year	Previous findings			Present findings			
				Blood urea-nitrogen	Urine	Culture	Clinical and X-ray	Blood-calcium	Blood-phosphorus	Blood-phosphatase
1	M.	59	Pyelolithotomy (1931) (L.)	26.0	Pus		No calculus. (Malignant prostate)	13.2	1.85	6.1
2	M.	14	Nephrectomy for multiple renal calculi (1928)	16.6	Many organisms		No calculus opposite kidney	12.7	2.45	4.9
3	M.	37	Pyelolithotomy (1929) (L.)	21.4	Pus and R.B.C.s		No calculus	12.7	2.1	5.0
4	M.	29	Pyelolithotomy (1928) (R.)	25.3	R.B.C.s		No calculus	12.4	2.2	5.1
5	M.	—	Nephrolithotomy	—	—		No calculus	12.4	2.5	4.9
6	M.	—	Nephrolithotomy (1929) (R.)	—	—		Passed 6 stones year after. Now no calculus	12.3	—	—
7	M.	—	Pyelolithotomy (1930) (R.)	30.6	Pus R.B.C.s B. coli		No calculus	11.7	—	—
8	F.	—	Pyelolithotomy (1927) (L.)	17.8	—		No calculus	11.0	—	—
9	M.	—	Nephrolithotomy (1922) Nephrectomy (L.) (1926)	20.9	Pus and R.B.C.s		Grit passed 2 years ago. Now no calculus	11.0	—	—
10	M.	—	Nephrolithotomy (1925)	—	—		No calculus	10.4	—	—
11	M.	30	Nephrolithotomy (1933) (R.)	—	Pus and R.B.C.s		No calculus	10.3	—	—
12	M.	18	Pyelolithotomy (1933) (R.)	—	—		No calculus	10.3	—	—
13	F.	—	Pyelolithotomy (1930) (R.)	—	—		No calculus	10.1	—	—
14	F.	—	Pyelolithotomy (1935) (R.)	—	—		No calculus	9.3	—	—

TABLE IC.—DOUBTFUL RECURRENCE.

No.	Sex	Age	Operation and year	Previous findings			Present findings			
				Blood urea-nitrogen	Urine	Clinical and X-ray	Blood-calcium	Blood-phosphorus	Blood-phosphatase	
1	M.	—	Pyelolithotomy (1925) (L.)	—	—	? shadow lower end left ureter	10.7	—	—	—
2	F.	—	Nephrectomy (L.)	17.0	—	? tiny shadow on right side	10.5	—	—	—
3	F.	30	R. ureteral and renal calculi (1926)	17.3 18.1	R.B.C.s Staph. albus	Strongly suggestive of stone lower end rt. ureter	10.3	—	—	—

TABLE ID.—RECENT CASES (1936-37).

No.	Sex	Age	Operation	History	Year	Blood urea-nitrogen	Urine	Blood-calcium	Blood-phosphorus
1	F.	38	Bilateral renal calculi. Nephrolithotomy (L.)	Pain in loin 12 years	1936	—	Pus and a few R.B.C.s	12.6 (phosphatase 2.4)	2.4
2	M.	15	Nephrolithiasis. Hydronephrosis. Nephrolithotomy (R.)	Negative	1937	24.0	Few pus cells. No growth	12.1	3.9
3	M.	22	? renal colic. X-ray— No stone	Small stone one year ago	1937	—	R.B.C.s. No growth	11.6	3.5
4	M.	30	Nephrolithotomy (L. and R.)	Stone removed (R. 1932) (L. 1933)	1937	21.5	No growth	11.6	—
5	M.	40	Bilateral renal calculi. Pyelolithotomy (L.)	Pyelolithotomy (R. 1926)	1937	29.7 25.1	Pus	11.6	2.8
6	F.	45	Pain L. Nil abnormal found	R. nephrectomy for calculous pyonephrosis 1935	1937	34.6	Pus, staph.	11.4	—
7	F.	32	Pyelolithotomy (L.)	Pain in back five years, L. lumbar region, groin and back 2 years	1936	25.8	Few R.B.C.s. <i>B. coli</i>	11.2	—
8	F.	53	Calculus pyonephrosis (L.). Nephrectomy (L.)	Negative	1937	25.0	Blood, pus, albumin	10.9	4.3
9	M.	40	? renal colic. Possibly small stone lower end of ureter	Pyelitis (1932) Renal colic (1935) Stone (1935)	1937	25.8	No growth	10.8	—
10	M.	47	Nephrolithotomy (L.)	Negative	1937	18.9	<i>B. coli</i>	10.7	—
11	M.	31	Nephrolithotomy (R.)	Negative	1937	22.6	Blood, albumin	10.5	—
12	F.	44	Multiple large calculi both kidneys	—	1936	—	—	10.4 (phosphatase 3.0)	2.7
13	F.	53	Nephrolithotomy	3 months pain	1936	24.6	No growth	10.0	—
14	F.	31	Bilateral renal calculi. Left pyonephrosis. Nephrolithotomy (R. and L.)	Negative	1937	31.8 24.5	Pus, <i>B. coli</i>	9.8	—
15	M.	31	Ureterolithotomy (R.)	1 year pain and haematuria	1936	25.1	No growth	9.6	—
16	M.	46	Nephrectomy (L.). Vesical suprapubic lithotomy	—	1936	—	No pus	9.5	—

TABLE IE.—RECENT CASES WITHOUT STONES NOW AND WITHOUT DEFINITE HISTORY OF STONES.

No.	Sex	Age	Diagnosis	Operation	Year	Blood urea-nitrogen	Urine	Blood-calcium	Blood-phosphorus
1	M.	46	Papilloma of bladder	Pyelonephritis (1929). R. nephrectomy. Pap. bladder (1932)	1937	36.4 25.1	Pus, <i>B. coli</i>	12.9	—
2	M.	28	L. renal colic. X-ray neg.	Hydronephrosis (R.). 1934 kidney decapsulated	1937	25.9	No growth	12.1	3.5
3	M.	62	Renal colic	Attack of renal colic 4 years ago	1937	36.3	Albumin. Few R.B.C.s. No growth	11.7	3.3

*Group II.*—In cases with enlarged prostate which came to our notice, blood-calcium determinations were made, and in some cases, blood-phosphorus also. The results are shown in Table II.

*Group III.*—In cases in the medical wards whose renal function was examined, determinations of blood-calcium were also made, and in a few cases, blood-phosphorus and phosphatase also. The renal function test employed was the determination of the rate of urea clearance according to the modification previously described by one of us (F. S. F., 1934). The results are given in Table III. The figures for blood urea-nitrogen in this table are not those obtained during the urea clearance determination, since the latter show the urea content of blood during the second hour following a dose of urea and are in excess of figures obtained when no urea has been given.

TABLE II.—ENLARGED PROSTATE.

No.	Age	Urine	Blood urea-nitrogen	Blood-calcium	Blood-phosphorus	Other findings
1	67	—	26.8 45.4	13.7	—	—
2	62	No growth	25.0	12.3	4.9	—
3	70	<i>B. coli</i> , strep., diphtheroids	36.4 27.4	12.1	—	—
4	67	Pns, staphs., and <i>B. coli</i>	38.2 29.5 29.8 22.6	11.9	8.0	—
5	63	No growth	33.8	11.7	3.5	—
6	63	No albumin	30.2	11.7	4.0	—
		No pus	22.0			
7	76	—	24.5	11.6	—	—
8	77	No growth	27.6	11.6	—	—
9	65	Pus, <i>B. coli</i>	45.6	11.5	4.2	—
10	80	No growth	33.3	11.5	—	—
11	66	—	30.2 34.6 27.3	11.4	3.3	—
12	47	Pus, albumin	25.5	11.3	3.0	Urethral stricture. also enlarged
13	65	—	28.8	11.1	3.6	—
14	67	—	27.4 21.6	11.1	2.0	—
15	64	—	25.0	11.0	—	—
16	53	No growth	31.8 27.8 24.4 22.7	10.9	—	Vesical calculus removed. Prostate hard and fibrous—enlarged
17	50	Pus	26.6	10.9	—	—
18	76	Pus	31.8 25.9 34.0	10.8	—	Vesical calculus removed
19	68	No growth	29.3 25.1	10.7	—	—
20	65	No albumin No pus	34.8	10.6	—	—
21	—	—	30.1	10.4	—	—
22	82	A few pus cells and R.B.C.s	28.8	10.3	3.6	—
23	66	—	20.6	10.3	—	—
24	68	Albumin and pus	40.0	9.7	—	—
25	64	No growth	60.6 25.1	9.6	—	—
26	65	—	54.9 32.7 24.8 26.1	9.1	—	—
27	66	—	—	9.1	—	—

TABLE III.—MEDICAL CASES

No.	Sex	Age	B.U.N.	Clearance	Diagnosis	Blood-calcium	Blood-phosphorus	Blood-phosphatase
1	F.	56	30.6	35%	Acute nephritis (probably acute exacerbation of chronic condition)	12.0	—	—
2	F.	54	—	—	Chronic nephritis	11.9	3.4	1.4
3	M.	7	29.1	—	Chronic congenital renal fibrosis	11.8	3.3	3.7
4	M.	47	87.3	11%	Malignant hypertension	11.7	—	—
5	F.	67	28.1	26%	Chronic nephritis	11.7	—	—
6	M.	18	45.1	28%	Small stature and renal inefficiency. ? renal dwarfism, ? renal rickets	11.6	4.0	11.7
7	F.	12	22.7	64%	Hæmaturia. Pyuria. ? T.B. kidney	11.5	—	—
8	M.	56	32.1	38%	Nephrosclerosis	11.4	—	—
9	M.	31	—	51%	Gastric ulcer; chronic nephritis	11.4	—	—
10	F.	53	38.0	37%	Chronic nephritis	11.4	—	—
11	M.	64	38.0	37%	Chronic nephritis	11.4	—	—
12	M.	52	23.5	64%	Cerebral hemorrhage. Hyperpiesia	11.3	—	—
13	F.	9	48.0	29%	Congenital renal disease	11.2	4.0	6.0
14	F.	48	—	39%	Chronic nephritis	11.1	—	—
15	M.	52	32.0	31%	Gastric ulcer; chronic nephritis	11.1	—	—
16	M.	44	31.4	55%	Nephrosclerosis	10.8	—	—
17	F.	37	—	49%	Subacute nephritis	10.7	—	—
18	M.	40	47.0	29%	Chronic nephritis	10.5	—	—
19	F.	39	33.4	9%	Nephrosclerosis. Obesity	10.5	—	—
20	M.	24	53.3	44%	Mild acute nephritis. Recovering	10.4	—	—
21	M.	44	30.5	48%	Nephrosclerosis	10.3	—	—
22	M.	35	—	38%	Chronic nephritis	10.1	—	—
23	F.	60	26.0	55%	Pyelitis	9.9	—	—
24	M.	58	42.1	56%	Chronic nephritis	9.8	—	—
25	M.	47	76.4	17%	Chronic nephritis	9.6	—	—
26	M.	33	58.2	25%	Acute nephritis	9.5	—	—
27	M.	31	42.9	32%	Acute nephritis	9.2	—	—
28	M.	51	48.5	26%	Chronic nephritis	9.2	—	—
29	M.	36	22.5	51%	Chronic nephritis	8.7	—	—

Eight cases, not showing evidence of renal disease, gave values for blood-calcium between 9.7 and 11 mgm.

#### SUMMARY OF RESULTS

Of the 10 cases in Table IA, three show values for blood-calcium exceeding 11.5 mgm., three show values lying within the suspicious range of 11-11.5 mgm. and four are within strictly normal limits; of the 14 cases in Table IB, seven show values for blood-calcium exceeding 11.5 mgm., and seven are within normal limits. Thus, so far as this small series of cases is concerned, there is no evidence of recurrence being specially associated with the raised blood-calcium figures. A combination of the figures of Tables IA, B, and C, shows the following:—

		TOTAL CASES—27.				Urine		
		Blood-urea			Evidence of infection positive	Evidence of infection negative	No evidence	
		Cases	Raised (cases)	Normal (cases)				
Calcium over 11.5 mgm. ...	10	6	2	2	5	2	3	
Calcium 11-11.5 mgm. ...	8	—	2	1	1	2	0	
Calcium not over 11 mgm. ...	14	1	6	7	5	1	8	

The incidence of infection, so far as we have evidence on this point, is practically the same in the raised and the normal blood-calcium groups. There is, however, a notable difference in blood-urea findings in these two groups; the cases with raised blood-calcium contain a much greater proportion of cases with raised blood-urea than those with normal blood-calcium. Thus the results suggest that where renal function is disturbed to the extent that urea-retention becomes evident, a tendency for raised blood-calcium to be found subsequently is greater than where such disturbance of renal function is not evident. Tables ID and IE show the following:—

TOTAL CASES—19.

	Cases	Blood-urea			Urinary infection		
		Raised	Normal	Not stated	Evidence positive	Evidence negative	No evidence
Calcium over 11.5 mgm.	8	4	2	2	3	5	0
Calcium 11-11.5 mgm.	2	2	0	0	2	0	0
Calcium not over 11 mgm.	9	3	4	2	3	5	1

The incidence of raised blood-calcium in these cases is substantially the same as in the previous ones. They are only "recent" cases so far as this investigation is concerned; an examination of the histories of those with raised blood-calcium shows that the great majority had signs or symptoms of renal trouble for a considerable time.

The incidence of infection, though considerably different from that noted in the previous cases, is nevertheless substantially the same in the raised and the normal blood-calcium groups.

There is again an appreciable difference in the distribution of raised blood-urea figures, the proportion of those with raised blood-calcium being decidedly greater than those with normal blood-calcium.

In the cases of Tables IA, B, and C, the data relating to the blood-urea and urine were obtained some time before the blood-calcium, whereas in the cases in Tables ID and IE all data were obtained about the same time. Hence a combined summary of all the cases in Group I can only be interpreted in a very general way, if at all. We have ventured to include such a summary, however, for what it is worth, as the figures showing the relationship between blood-calcium and blood-urea, and blood-calcium and infection, seem to be of interest. It is as follows:—

TOTAL CASES—46.

	Cases	Blood-urea			Urinary infection		
		Raised	Normal	Not stated	Evidence positive	Evidence negative	No evidence
Calcium over 11.5 mgm.	18	10	4	4	8	7	3
Calcium 11-11.5 mgm.	5	2	2	1	3	2	0
Calcium not over 11 mgm.	23	4	10	9	8	6	9

The figures for blood-phosphorus have not been specially tabulated, since they are confined almost entirely to the cases with raised blood-calcium. The majority of these fall below 3 mgm., and two are below 2 mgm., i.e. there is a tendency for raised blood-calcium figures to be associated with rather low phosphorus figures.

All the phosphatase figures are within normal limits.

A summary of the results in Table II shows the following:—

TOTAL CASES—27.

	Cases	Blood-urea			Urinary infection		
		Raised	Normal	Not stated	Evidence positive	Evidence negative	No evidence
Calcium over 11.5 mgm.	8	5	3	0	2	4	2
Calcium 11-11.5 mgm.	6	6	0	0	9	1	3
Calcium not over 11 mgm.	13	11	1	1	4	4	5

In this group the proportion of cases with raised blood-urea is much greater than in the previous group, and there is no obvious association of raised blood-urea with raised blood-calcium; indeed, so far as this small series is concerned, the reverse is the case. This is not surprising as practically all patients were suffering from retention on admission and the level of the blood-urea before the relief of obstruction is not a very reliable index of the real condition of the kidneys. There is again no definite evidence of a special association between infection and blood-calcium level.

The blood-phosphorus figures in this group, even where the blood-calcium is raised, are mostly normal. This failure to find high blood-calcium associated with low blood-phosphorus may perhaps be due to the condition of retention present in these patients.

A summary of the results in Table III shows the following:—

TOTAL CASES—29.			
Calcium over 11.5 mgm.	...	...	6
Calcium 11-11.5 mgm.	...	...	9
Calcium not over 11 mgm.	...	...	14

Of the four blood-phosphorus figures in this group, two must be considered low, in view of the age of the patients; of the four phosphatase figures, three are normal and one slightly raised.

#### DISCUSSION

The first fact of importance which emerges from these results is the absence of any marked preponderance of high blood-calcium figures among the cases with recurrence of renal calculi compared with those without recurrence. If raised blood-calcium is to be considered as an evidence of a primary hyperparathyroidism which is the cause of calculus formation, the removal of the calculi would not remove the hyperparathyroidism and recurrence should occur, and raised blood-calcium persist in such cases. Yet in a number of cases raised blood-calcium is found, though no recurrence has occurred over periods of a number of years; and on the other hand recurrence has occurred in a number of cases in which there is no evidence whatever of hyperparathyroidism. It is true that, so far as the latter are concerned, it might be claimed that any rise in the blood-calcium due to hyperparathyroidism may have been opposed by a tendency to reduction of blood-calcium due to secondary renal damage caused by the stones. The evidence is, on the whole, however, against the view that hyperparathyroidism is the cause of the stone formation.

Probably the most important fact which our results bring to light is the occurrence of a definitely raised blood-calcium in three entirely different groups of cases in which the kidneys are involved, and the proportion of raised blood-calcium figures is not greatly different in these groups. Indeed, if figures over 11 mgm. are considered, it will be seen that the proportion is remarkably constant in the three groups, viz. about 50%. Whatever figure may be accepted as the upper normal limit for blood-calcium, we think it will be generally agreed that the proportion of figures from normal individuals which exceed 11 mgm. is considerably less than this. Hence our results show that there is undoubtedly a tendency towards increased blood-calcium in widely different types of disease involving the kidneys. It seems fair to conclude, therefore, that the one factor common to all these conditions, namely involvement of the kidneys, is responsible for the rise in blood-calcium which has been demonstrated.

Hence the raised blood-calcium which may be found in association with renal calculi is in general the result of renal damage, and the previous suggestion that it is not evidence of a primary hyperparathyroidism which is the cause of the formation of calculi, is confirmed.

Castleman and Mallory found that the average duration of symptoms of their cases showing only renal stones was 3.2 years, whereas the average duration in the cases with classical bone lesions was 8.6 years. Of our own calculus cases which show

a raised blood-calcium, in three a period of ten or more years has elapsed between the first operation for stones and the present examination, in two a period of eight years, and in five a period of seven years. Since all these periods date from a first operation they will be shorter than the periods covering the duration of symptoms. Any of these 10 cases, therefore, if due to primary hyperparathyroidism, might have developed the true bone lesions of generalized osteitis fibrosa, and it is reasonable to expect that at least one or two would have done so. The absence of such bone changes is therefore additional evidence against the view that a primary hyperparathyroidism is the cause of the renal calculi in these cases.

Our results, by showing that blood changes which might be considered as evidence of hyperparathyroidism may be found in association with renal disease, form an interesting corollary to the anatomical findings of hyperplasia of the parathyroid tissue in renal disease which have already been referred to. Whether the rise in blood-calcium in renal disease is really due to a hyperparathyroidism caused by such disease, or is a more direct consequence of disturbance of renal function is perhaps open to dispute, but this does not affect the conclusions we have arrived at regarding the relation between renal calculi and raised blood-calcium.

The changes in blood-calcium and blood inorganic phosphorus which are generally associated with renal disease are a decrease in the calcium and an increase in the phosphorus; actually such changes are not usually demonstrable until the renal disease is considerably advanced, and are generally considered to indicate a grave prognosis. In milder degrees of renal disease, although changes of this nature may not be demonstrable, the tendency towards such changes will no doubt be present. This tendency may act as a stimulus to the parathyroids to increase their normal activity to counteract it, and this increased activity, if maintained for any length of time, must result in hyperplasia. It is in this way that Albright *et al.*, as we have already pointed out, explain the parathyroid hyperplasia found in renal disease, and we see no reason to disagree with this explanation. As the renal disease progresses, the tendency towards low blood-calcium and high blood-phosphorus would appear to increase to a point beyond which it is impossible for the parathyroids to neutralize it, so that the blood changes of advanced renal disease become manifest. We see, therefore, in parathyroid hyperplasia, an explanation why the actual appearance of low blood-calcium and high blood-phosphorus is postponed to the late and severe stages of renal disease.

It would appear from the results we have just presented, however, that in the earlier stages of renal disease the response of the parathyroids to its stimulus results, in a certain proportion of cases, and/or for a certain length of time, in an enhanced activity of these glands which is rather more than sufficient to counteract the tendency arising from the renal disease, so that raised blood-calcium (and to a less extent, reduced blood-phosphorus) make their appearance. It is even conceivable that occasionally the response of the parathyroids to this stimulus to hyperplasia may be so excessive as to give rise to the changes associated with generalized osteitis fibrosa.

This explanation of the results found in the cases we have investigated is not, however, as we have already hinted, the only one which might be offered, but we feel that a full discussion of the alternative views would be out of place in the present communication. We do not deny the possibility that the presence of renal calculi may sometimes be an early manifestation of true, primary, hyperparathyroidism, but in actual fact we consider that this can be true of only a very small proportion of cases—certainly so small that an operation for the discovery and removal of parathyroid tumours in all cases of renal calculi is entirely unjustified. Nevertheless, this possibility should be borne in mind, and in cases of renal calculi signs and symptoms of parathyroid tumour should be carefully looked for, and removal of the tumour attempted if positive evidence is forthcoming.

We desire to express our thanks to Professor E. R. Flint for allowing us to investi-

gate cases of renal calculi formerly under his care and to other colleagues of the Honorary Staff of the Leeds General Infirmary for access to their cases and case records.

#### REFERENCES

ALBRIGHT, F., BAIRD, P. D., COPE, O., and BLOOMBERG, E. (1934), *Am. J. M. Sc.*, **187**, 49.  
 CASTLEMAN, B., and MALLORY, T. B. (1935), *Am. J. Path.*, **11**, 1.  
 FOWWEATHER, F. S. (1934), *Quart. J. Med.*, **5** (new series), 63.  
 GILMOUR, J. R., and MARTIN, W. J. (1937), *J. Path. and Bact.*, **42**, 431.  
 JENNER, H. D., and KAY, H. D. (1932), *Brit. J. Exper. Path.*, **13**, 23.  
 MCKAY, E. M., and MCKAY, L. L. (1927), *J. Clin. Investigation*, **4**, 295.  
 PAPPENHEIMER, A. M., and WILENS, S. L. (1935), *Am. J. Path.*, **11**, 73.  
 PETERS, J. P., and VAN SLYKE, D. D. (1931), "Quantitative clinical chemistry", vol. i, 1097.  
 RUSSELL, D. S. (1929), Medical Research Council Sp. Report Series, No. 142, p. 161.

MR. H. P. WINSBURY-WHITE: It is clear from what Mr. Pyrah has said that the interpretation of raised blood-calcium is not necessarily a simple problem.

The changes in bone so often present in cases of parathyroid disease represent yet one more example of a number of pathological conditions of bone which are sometimes associated with urinary lithiasis. The importance of the relationship between disease in the osseous system and urinary lithiasis is obvious when we remember that the bones are the storage places for the great bulk of calcium in the system, and that calcium is by far the commonest chemical constituent of urinary calculi.

It is reported by several observers, with regard to parathyroid disease in its relationship to urinary lithiasis, that the condition of renal calculi is always unilateral. This makes it perfectly clear that, in addition to the distant disturbances which raise the blood-calcium and which encourage the formation of stone, there must be some local renal condition which induces stone to form in one kidney and not in the other.

### The Association of Nervous and Urinary Disease

By A. RALPH THOMPSON, Ch.M., F.R.C.S.

THE basis of this paper is my own clinical experience, coupled with the notes of a large number of post-mortem cases which were collected many years ago. These have been most useful in confirming or contradicting clinical opinions. The paper is not a statistical one, nor is it intended to record how often urinary complications occur with nervous diseases, and especially tabes.

*Tabes*.—In this disease retention of urine may be the first symptom noted by the patient, and three illustrative cases may be cited who were all busily and usefully employed when they came under observation. Although retention was the first symptom noted by these patients, yet in all of them were the Argyll-Robertson pupils present and the knee-jerks absent. One of these cases lived for at least ten years after he was first seen by me.

The diagnosis may show some difficulty. The bladder, which may be holding a good deal of urine, say 1,200 c.c., is often not easily palpable, and being so distended pushes the prostate down into the rectum, which gives the impression that the condition is due to simple enlargement of the gland. On removal of the fluid this enlargement disappears. Another point is that tabes in a few cases may be accompanied by a stricture of the urethra, with the result that the nervous lesion is overlooked. There are notes of 12 such cases, one post-mortem and 11 clinical. Of the clinical cases one was situated at the meatus, and for this reason may have been primary syphilitic in origin. This occurrence of a stricture with tabes is very important for two reasons. First, it makes difficult the passage of a catheter to relieve the distension of the bladder, and secondly it predisposes to sepsis in a bladder peculiarly susceptible to infection. The stricture must be treated adequately. Its presence can only add to the troubles of the tabetic, which include not only back pressure upon the bladder

but also upon the kidneys. At one time some French authorities taught that stricture was the cause of tabes, but few, if any, would hold that opinion nowadays. In this series of cases there was one most satisfactory result from treating the stricture by dilatation. The patient suffered from lightning pains in both loins. When the stricture had been fully dilated up to 18/22 French size, he lost his lightning pains entirely, though he still showed other signs of the disease. In this case the stricture may have led to back pressure upon the kidneys, which may have been partly responsible for this manifestation of tabes. Also it is a matter of experience how very much better patients are who have a stricture dilated, and in tabetics it is of importance to improve their general health, which may be done by the dilatation of a stricture should one be present. In two other cases there was not only an improvement in the general health but also in the ataxic gait.

If then these facts be borne in mind, it may be said that in tabes, the presence of a stricture must be excluded. If one is discovered it should be treated adequately by dilatation.

The following clinical forms of cystitis may be found in tabes. First there is the haze of urine that is associated with "bacilluria"; secondly there is a definite pyuria, and thirdly aropy pyuria where the deposit of pus is very thick, much thicker than occurs in cystitis without tabes. Fourthly there may be blood. Blood in the urine in an ordinary case of cystitis may be a very serious symptom, but in tabes it would not appear to be of such importance. In fact in some cases the patient may note haematuria as the first and only symptom, and the urine may or may not contain clots. Fifthly there may be faeces in the urine. We must examine for tabes in all cases of stricture or of cystitis, and we must examine for stricture in all cases of tabes.

Before more particular notice is taken of tabetic cases with urinary complications, it will be useful to indicate the various forms of ascending nephritis that occur following upon sepsis in the lower urinary tract. Marcus Beck and Kenneth Walker have insisted on the lymphatic passage of infection from the lower urinary tract to the kidneys. Ascending nephritis is, in fact, commonly an acute interstitial nephritis spreading by the lymphatics of the urethra to the base of the bladder, and thence along the wall of the ureters to the capsule and interstitial tissue of the kidneys. Any changes that occur in the mucous membrane of the upper parts may be regarded as secondary. Ascending nephritis is then frequently an ascending lymphangitis, and as with lymphangitis in other situations local abscesses may form in these cases anywhere between the urethra and the kidneys. Thus in my notes there are recorded cases of prostatic abscess, and abscess between the rectum and the bladder, an abscess between the cæcum and the bladder, or between the colon and the bladder, or on the deep aspect of the sheath of the psoas muscle, or around the kidney itself, and finally above the kidney, and between that organ and the diaphragm.

Thus in some cases the first trouble noted by the patient who is suffering from tabes may be the presence of an abdominal abscess secondary to an ascending lymphangitis, which is passing upwards towards the kidneys.

Furthermore, just as ascending nephritis may be unilateral in ordinary cases without tabes, so with tabes only one of the kidneys may be affected and, more than this, the sound one may show compensatory hypertrophy.

There are notes of a case of prostatic abscess at autopsy, with a nervous origin of the trouble in the urinary tract, and one clinical case may be suspected of the association of an abscess in the prostate with tabes, of which disease certain signs were present clinically, and he died with the prostatic abscess. There is one case of advanced cystitis with faeces in the urine, and at operation it was found to be due to a fistula having formed between the cæcum or the colon and the bladder. The appendix was healthy. An abscess may have formed in this case between the gut and the bladder, and opened into both viscera. The patient was one of those who had stricture as well as tabes. This form of cellular sepsis may be followed by femoral

thrombosis and pulmonary embolus, as in one post-mortem case of disease of the spinal cord that was undiagnosed. Further than what has been noted, stones may occur in the urinary tract. The following case seems to show, in addition to the presence of stones, that one kidney may have been infected long before the other. The left kidney was at the post-mortem found to be pyonephrotic, and there was a phosphatic stone in the left ureter, and two in the bladder. It was in the right kidney that later changes had occurred, for this kidney showed no loss of cortical substance which, however, contained many abscesses, and its pelvis was dilated.

A third case is noted in a patient who had lived for eighteen years after a fracture-dislocation of the second lumbar vertebra, which had led to pressure upon the cauda equina. At the autopsy it was recorded that he had had incontinence, and stones were found in the bladder, and whilst the prostate was the seat of an abscess yet only one kidney was affected, and the other was compensatory.

An important point in connexion with possible sepsis in certain cases of injury to the spinal cord (apart altogether from tabes) is that abdominal urinary organs may be damaged by the same accident that led to the damage of the cord, and this should be remembered if the question of instrumentation should arise.

Ascending nephritis that occurs without tabes is not necessarily fatal, and I have had two cases in which it occurred which have done well after an appropriate operation, one a case of fractured pelvis, and the other a case of congenital stricture of the urethra.

The cystoscopic appearance of the tabetic bladder can hardly be said to be very characteristic. In one case which was examined when the bladder was distended the mucosa was found to be pale and stretched, whilst in two other cases in whom the examination was conducted with only 5 oz. of fluid in the bladder, there was found basal cystitis, and trabeculation of the bladder wall.

Attention may now be directed to the question of the treatment and prognosis of cases of tabes with urinary complications.

As to the treatment, there would seem to be a clear indication for an instrument to be used when there is cystitis, and when there is a stricture, even though there is no actual cystitis. If only a stricture has to be treated with tabes, then a metal bougie should be used. It should be of such a size as will pass the stricture easily. Damage may be fatal when it occurs in the urethra, and the gentle hand is of far more value than meticulous attention to asepsis. Blood drawn in a case of tabes with stricture is a most serious disaster. After it has been found that there is no stricture, or after the stricture has been dilated up to 18/22 French size, if the cystitis does not clear up, then a catheter should be passed and the bladder should be irrigated with some antiseptic such as 1/2,000 oxycyanide of mercury. When the bladder is not affected with inflammation, and the adnexa are clean, no instrument should be passed at all, and the patient should be allowed to pass what water he can with overflow. Of course if he is not passing the amount that he should do, then a catheter must be passed to empty the bladder twice a day, but frequency of passage of an instrument ought not to be accompanied by any undue roughness. Under no circumstances should the bladder be opened unless there is some local condition that demands it, such as will be mentioned shortly. Cases are noted in which the patient has been passing a catheter on himself for four and six years and the urine has remained perfectly clear. Needless to say, this local treatment is not the only one called for, as antisyphilitic treatment must also be adopted, and cases of cystitis undoubtedly improve with this additional form of treatment.

As to the prognosis, one case has been noted in which the patient lived for ten years after retention had been diagnosed, and there are two cases in which five years of useful life occurred after cystitis had been set up, and kept in check.

Three cases of inflammation have been traced to the last. In the first the patient was pursuing his usual avocations till practically the end, and he died from ulcerative

colitis and exhaustion. In the second case the patient died, apparently of ascending nephritis, and the third patient who had "bacilluria", improved greatly after being treated with irrigation of the bladder following dilatation of a stricture, and the injection of salvarsan or one of its derivatives. His kidneys may, however, have become affected, for though he lost much of his ataxia, yet he died suddenly in the street one day, as a result of a stroke.

In one case there was quite a remarkable result, for ascending nephritis had been diagnosed, and when the patient was seen by me, I could not but agree with this diagnosis. The bladder was irrigated and the patient lived for three years afterwards, and died in coma.

Tabes has been thus fully considered from the urinary point of view, partly because this disease is the commonest in my notes, and partly because it shows so well the urinary changes that take place with a nervous lesion. We have seen that tabes is occasionally associated with a stricture, and this should be treated for local, as well as general, reasons. We have seen that stricture may complicate the treatment, and its presence should be excluded, and if present its danger to the passage of instruments well recognized. We have seen that catheterization even by the patient himself may not be attended by bad results, and have explained this by the probable fact that no damage to the urethra has been caused. We have seen that mere retention may be best treated by being left alone provided that a sufficient amount of urine escapes by overflow.

Finally attention may be paid to the question of big operations in tabes. One case of growth of the bladder occurred with tabes and a suprapubic opening was made and the growth was removed, but it is noted that there was most inconvenient protrusion of the bladder wall. The patient died after the operation. There has been also noted another case of growth of the bladder with tabes, and its successful removal. The case of faecal fistula was operated upon, and a lateral anastomosis performed but though the patient survived the shock of the operation he succumbed within three weeks from the effects of ascending nephritis.

It may be considered that a lateral anastomosis of the bowel without removal of the fistula was an unwise step, but the case is quoted as showing that a tabetic may stand a big operation quite well. Mr. W. H. Ogilvie resected a large piece of bowel for growth of the colon in a tabetic case of mine with urinary symptoms, and the patient did well after the operation. From these few cases of a large operation in tabes it would appear that there may be no special risk attendant upon the tabes.

So far the question of retention with tabes has been considered, and now there may be considered those cases in which the bladder is over-active, and passing all its water. In this connexion no attention will be paid to injuries of the spinal cord, as that has already been done by the late Sir John Thomson-Walker, but in this connexion some of the cases of myelitis with spastic paraplegia and of incontinence due to over-activity of the bladder muscle, will be considered. In a case of injury, which must be mentioned, and in which autopsy was performed, some softening of the cord was found at the level of the 7th cervical vertebra. The bladder, in this case, was found to be small and hard and congested. In some of the cases in which myelitis was noted there was constant passage of urine from a small bladder, accompanied in many cases by want of control over the rectum. In two such cases great improvement followed upon instillation into the bladder of sodium bromide 20% solution. In one of the cases there was no recurrence of the incontinence after eighteen years, though the incontinence of faeces continued. Except for the purpose of such instillation, there is no need for an instrument to be passed. When all the water is being passed, care should be taken to ensure that it is received into some suitable antiseptic receptacle.

*Neurosis.*—A quite different group of cases may now be considered, namely the functional cases with urinary symptoms. We may ask ourselves these questions in

this connexion. Are we quite sure that the trouble is functional ? And if the trouble is associated with definite lesions are the functional conditions going to be improved by their removal ? Philosophy may make a diagnosis in such cases, but it is enthusiasm which will bring about a cure. In this connexion it will be well for us to recollect that extraneous diseases may lead to urinary symptoms and even urinary involvement, thus it is well known that many of the cancerous growths of the kidney come from outside that organ. Cardiac lesions may lead to haematuria. Cirrhosis of the liver with or without ascites may lead to frequency of micturition, and tuberculous or calcified glands may press upon the kidney or its duct, and lead to painful passage of urine along the ureter. Women's complaints also are well known to produce urinary symptoms, and in this connexion there are several cases in my notes where a prolapse of the bladder did not appear to be associated with an accompanying prolapse of the vagina.

In this connexion, too, we must remember that most serious disease may occur with neurosis. Thus there are notes of cases in whom a neurotic condition was highly developed who had in addition, in one case, aortic disease which ultimately proved fatal, and in another case, although injections of water were found useful in allaying the very great pain, yet the patient died with a most painful condition, namely a large spinal sarcoma. We may ask ourselves if patients do not only die *with*, but *of*, neurosis, and there are notes of three cases in my clinical records where this has been suspected, namely that they have died from the neurosis. The first case was in a nurse who thought she was passing pus in the urine. It was in fact found to come from the vagina, and she was operated upon for a suspected left kidney ; she died three days after the operation. There was only a small patch of lobar pneumonia in one lung. There is an autopsy note of a case in which a patient had actually coloured the urine in order to deceive her medical attendant ; she was operated upon, and died shortly after the operation. No lesion was discovered at the post-mortem. I have myself operated upon a man with a growth of the bladder ; no specially severe operation was done, but he died some six days after the operation. No cause was discovered at the post-mortem examination, and there had been no obvious shock after the operation.

In connexion with the treatment of these cases it is very necessary that there should be complete liaison between all the medical men concerned in any particular case. There is in the notes the record of a woman who consulted me on account of frequency of micturition. There was some slight amount of scarring at the neck of the bladder and the adjacent part of the vagina, and it was recorded that she had had difficulty with a birth some two years before. There were also tuberculous or calcified glands which were adjacent to the left ureter. After a report had been made to the husband and the medical attendant they wrote in reply that they regretted that nothing more was found. I do not suggest that the trouble was not chiefly functional, but I wonder if either of the men concerned would have thought so little of a ring of fibrous tissue in his own urethra !

#### SUMMARY

In this paper attention has been drawn to retention in cases of tabes, and its not uncommon association with a stricture of the urethra.

Forms of ascending nephritis have been indicated, and cases of tabes have been followed to the last.

Efforts have been made to indicate the prognosis in tabes with urinary involvement as well as the proper treatment, and in some cases the results have been encouraging.

Attention has also been drawn to the over-active bladder which occurs with spastic paraplegia and with myelitis.

Finally, attention has been paid to certain functional cases.

[November 25, 1937]

## Two Cases of Torsion of the Testicle

By H. P. WINSBURY-WHITE, F.R.C.S.

BOTH these cases were in young adults, one aged 20, the other aged 21.

In each case the affected testicle was in the scrotum. The onset of the symptoms was insidious and no predisposing cause could be identified. In neither case was there a history of urethral discharge. Examinations of the urethra, prostate, and urine all failed to supply any evidence of infection. Nevertheless in each case the physical signs strongly suggested an inflammatory condition, as the overlying skin was red, and there was visibly a swelling within the scrotum which on palpation was found to be the corresponding testicle enlarged to several times its normal size. It was difficult to define the epididymis from the body of the testicle, and it was characteristic in both cases that the tenderness was less than one would expect in an inflammatory condition of such a size. From this stage onwards the two cases diverged with regard to the courses they took, for in one, an area of softening developed on the upper and anterior aspect of the scrotum, and this strongly suggested a suppurative change in the underlying testicle which was adherent to the skin in this locality. There was, however, no pyrexia.

On incision of the fluctuating area, no pus or caseous material escaped, but a mass of blood-stained testicular débris was evacuated. This was identified microscopically by the pathologist, who also added that the substance of the testicle showed widespread extravasation of blood.

About a week later I carried out orchidectomy and a dissection of the extirpated organ proved very interesting.

The testicle was enlarged to about two or three times its normal size, its cut surface was uniformly blue-black in colour, and, on pressure, serum stained with dark blood, oozed from the whole of the cut surface. The general appearance strongly suggested a condition resulting from obstruction to the venous return from the testicle. The report on a section of this testicle by Dr. Scott-Wilson, was as follows:—

"This portion of testis is completely necrotic, and shows a generalized severe interstitial and intratubular haemorrhage. At one edge the necrotic tissue is undergoing organization into fibrous tissue. One of the tubules contains a purulent exudate, but I consider this to be secondary to the necrosis. There is no acute inflammation in the specimen, and no local cause of the necrosis is discoverable. The appearances suggest that there may have been some interference with the blood supply, possibly at a distance from the organ."

In seeking a cause for the condition found I was unable to identify any twist in the spermatic cord. It is possible, however, that in removal of the testicle an existing turn may have been undone. I was impressed by the condition at the junction of the cord with the testicle, for the cord seemed to be closely surrounded by a collar of oedematous testicular tissue and almost buried in it, and I found, in dissecting-out the structures of the cord, that they seemed to be invaginated in some curious way into this mass of tissue. This condition was very likely causing an obstruction to the veins of the cord.

In the other case no softening occurred, but the swelling gradually subsided so that three months after the onset the testicle was smaller than its fellow, and was apparently the seat of a fibrosis, judging by its consistence, which was uniformly firm.

These two cases are similar in several respects to many reported in the literature, for it is recorded that about 75% occur in adolescents or young adults, and the onset is generally insidious—in fact in three cases the condition is said to have come on during sleep. The absence of a predisposing cause was also a general feature, and at the outset the condition was almost invariably taken to be inflammatory, while in those cases in which the testicle was not removed, testicular atrophy was the

common sequel. It seems to me, however, that the distinction between torsion and inflammation is rather of academic than of practical interest, for in either case the treatment should obviously follow conservative lines, unless there is evidence of a disintegration of testicular substance.

**Seminoma of Testis.**—J. G. YATES BELL, F.R.C.S.

This specimen of seminoma of the testis was removed at operation from a boy, aged 16, who had a history of bilateral incomplete descent of the testes. He had been treated with thyroid and pregnyl injections, and as a result the left testicle had descended one year previous to operation. The swelling had not been noticed by the patient and was only discovered accidentally by the doctor when examining to note the state of the undescended right testicle. Orchidectomy was performed and followed by X-ray therapy to the lumbar glands and chest. The right testicle is still undescended.

*Microscopical report* (Dr. E. ff. Creed): The tumour is a seminoma with extensive areas of necrosis. The cell type appears uniform throughout, but the structural details are obscured by degenerative changes. The neoplastic cells are arranged in sheets and are polyhedral. They have a reticular cytoplasm and large vesicular nuclei with well-marked nucleoli. Mitoses are numerous; some are irregular. A few multinucleate cells are present. The tumour has a very scanty stroma. There are some collections of lymphocytes, particularly in the neighbourhood of blood-vessels.

I think that this case should be placed on record, as the malignant disease was noted one year following descent of the testicle after a course of pregnyl injections. Whether or not this hormone may have had some predisposing part in the onset of the malignant disease it is not possible to say, but it is not impossible by analogy with the effects of oestrin injections in animal experiments. Another possible explanation is that malignant disease was present before descent and the increased weight of the testicle helped full descent. Against this, however, is the doctor's statement that the testicle had only increased in size some time after the full descent was obtained.

## Section of Radiology

President—R. E. ROBERTS, M.D.

[November 19, 1937]

### DISCUSSION ON RADIOLOGY AND CHEST SURGERY

**Mr. Hugh Reid:** It is to their radiological colleagues that surgeons owe the enormous impetus which has been given to chest surgery in recent years.

The subject is now so extensive that I thought it advisable in this discussion to deal chiefly with the surgical treatment of tuberculous cavities in the lung. In this way the effect of chronic inflammations on the pulmonary and mediastinal structures can be considered and the value of such procedures as diaphragmatic paralysis, apicolysis, extrapleural pneumothorax, thoracoscopy and division of adhesions, pulmonectomy, thoracoplasty, and suchlike modern operative measures can be briefly exemplified.

It is recognized that healing of tuberculosis of the lung takes place, as in other organs of the body, by fibrosis. The chief factor in bringing this about, after the general resistance of the patient, is rest—physiological rest to the diseased organ.

James Carson of Liverpool, over a hundred years ago, was the first to suggest that by letting air into the pleural cavity the negative pressure could be overcome, and the lung would be enabled to contract and retract in very much the same way as the uterus does after parturition. This, of course, is the principle of artificial pneumothorax. The lung is put at rest and kept at rest by frequent refills, so allowing the focus of infection to heal.

*Thoracoscopy with division of adhesions.*—In some cases, however, a disappointing result is obtained, and when we look at the X-ray photograph the reason is abundantly clear. Stretching from the region of the cavity is a pleural adhesion, attaching it to the chest wall and holding out the lung. It is in such cases that thoracoscopy with division of adhesions is indicated. The striking results can be clearly demonstrated by X-rays (fig. 1).

In certain cases, however, it is not a question of a few adhesions, but of massive adhesions—a symphysis between the visceral and parietal pleura.

*Thoracoplasty.*—Now is the time to contemplate the operation of thoracoplasty. This operation has an interesting history; it has been through many vicissitudes, and is still evolving. The indications must be quite definite; the disease must be of the productive (or fibrotic) type, and the contralateral lung must be sound. The technique itself varies in the hands of different surgeons. The completed operation shows removal of the 1st and 2nd ribs, and about 12 cm. of the remaining fixed ribs. This causes the chest wall to collapse on to the lung and bring about permanent rest. Controversy still ranges over the question of partial thoracoplasty either of the upper or the lower ribs for a localized lesion in the upper or lower lobes of the lungs (fig. 2).

*Pneumolysis.*—Corresponding to a partial upper-lobe thoracoplasty is the operation of extrapleural pneumolysis with or without paraffin plombage. An opening is made in the back of the chest wall outside the parietal pleura, and the resulting

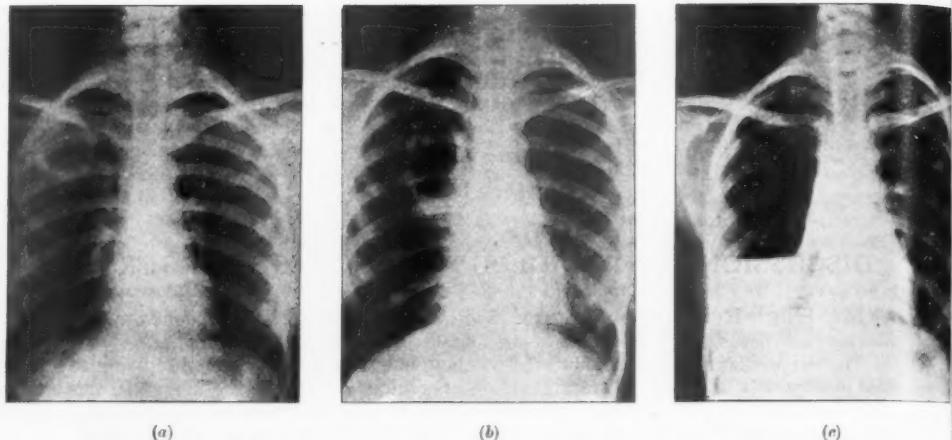


FIG. 1 (Case A).—(a) Large right apical cavity. (b) Large right apical cavity after artificial pneumothorax and division of some adhesions. (c) Disappearance of large right apical cavity after division of all adhesions.

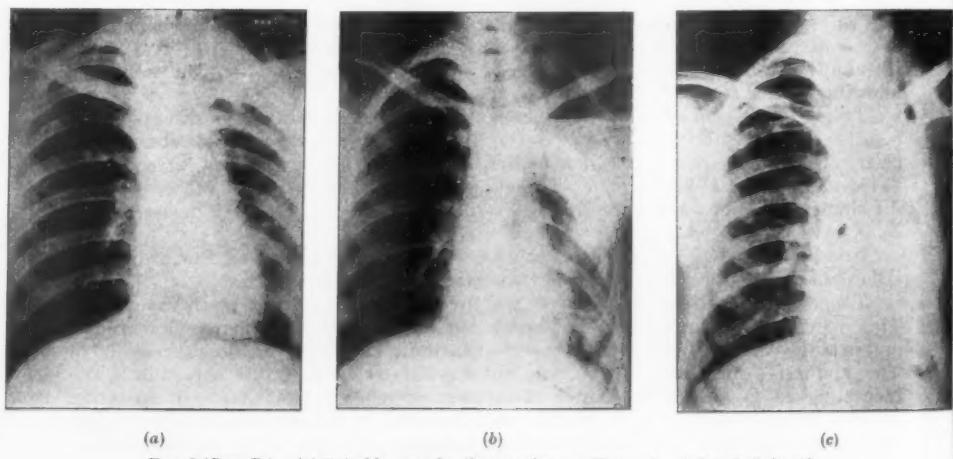


FIG. 2 (Case B).—(a) Suitable case for thoracoplasty. Extensive tubercle left side. (b) After first-stage thoracoplasty. (c) After second-stage thoracoplasty.

space is lightly packed with paraffin or filled with air. The walls of the apical cavity are thus brought into contact with each other, tension is released, and the tuberculous process is allowed to heal.

*Phrenic avulsion.*—Occasionally nothing more is required to give the lung the necessary amount of rest than avulsion of the phrenic nerve, with consequent paralysis of that side of the diaphragm. This operation is particularly useful in cases in which fibrosis and contraction are present and the cavity is small and thin-walled (figs. 3 and 4).

*Putrid abscess of the lung.*—An entirely different aspect of lung surgery is the diagnosis and treatment of abscess of the lung as apart from a tuberculous cavity.

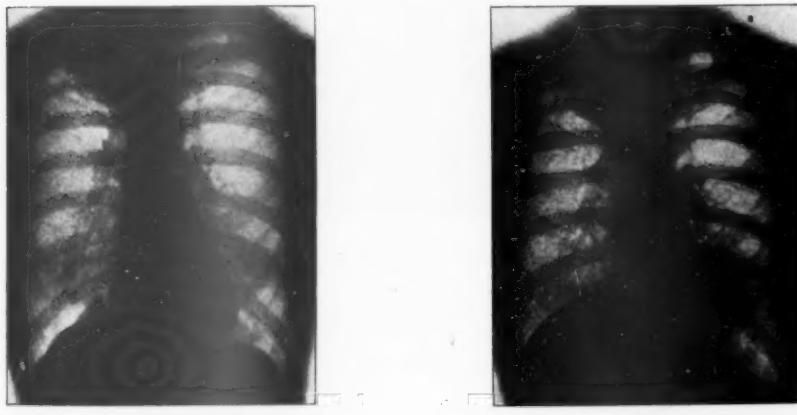


FIG. 3 (Case A.G.).—Aged 61. Result of phrenic avulsion for apical cavity.  
(a) Before treatment. (b) Three weeks after operation.

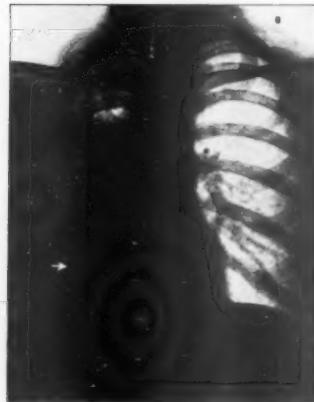
Localization is the all-important necessity. There is no special site of approach. The abscess must be approached where it is adherent to the parietal pleura. Several ribs may be required to be resected so that the whole of the roof can be removed, and the cavity fully opened up and packed with gauze. At all costs the pleural cavity must not be opened and infected. If adhesions are not found an extrapleural pack must be left over the site, to cause adhesions, and the cavity opened up at a later date.

*Carcinoma of the lung.*—Carcinoma of the lung is a special subject in itself. Every diagnostic method at our disposal must be used, and particularly lipiodol injection of the bronchial tree to demonstrate a blocked bronchus (figs. 5 and 6).

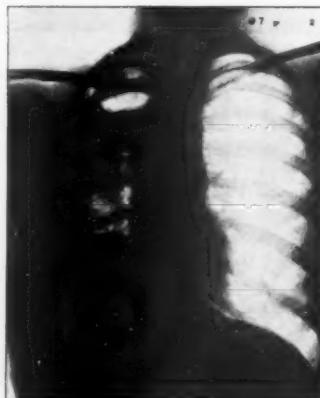
In the last few years methods of treatment such as bronchoscopic aspiration, cautery drainage, thoracoplasty, plombage, phrenic avulsion, artificial pneumothorax, &c., have narrowed themselves down to lobectomy either in one or two stages.

Innocent tumours, hydatid cysts, foreign bodies, and other conditions of the lung, need not be considered separately in this review because they do not necessitate the use of further principles not already mentioned.

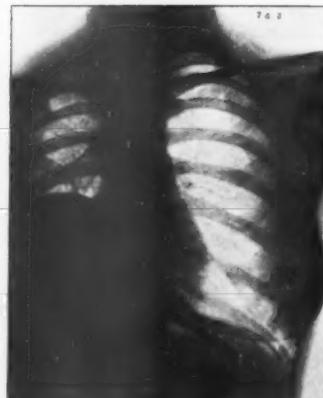
In conclusion we must remind ourselves again that clinical methods must not be neglected. However dazzling our X-ray methods may be—and they are indeed dazzling—the stethoscope, palpation, and auscultation of the chest, together with a careful history of the case, must be given their rightful place, and they will often be the deciding factors in the final issue.



(a)



(b)



(c)

FIG. 4 (Case G.S.).—(a) Results of phrenic avulsion. (b) Three weeks after.  
(c) Eight and a half months after.



FIG. 5 (Case C.).—Carcinoma of lung, after lipiodol injection, simulating (1) abscess (2) encysted empyema.



(a)



(b)

FIG. 6 (Case D.).—(a) Carcinoma of lung simulating abscess (lateral view). (b) Carcinoma of lung simulating abscess (antero-posterior view).

**Dr. J. V. Sparks:** As Mr. Reid has indicated, before the era of accurate radiological interpretation, thoracic surgery, as practised to-day, was not even attempted.

Mr. Roberts in his Lettsomian Lecture says that its late appearance was justified, as it is only during the present century that improvements in operative technique and additions to our means of accurate diagnosis have brought many intrathoracic diseases within reach of aid from the surgeon. He further states that the safety and success of a thoracic operation may depend upon the thoroughness with which an elaborate series of investigations has been carried out. In these investigations to which he refers, radiology plays an important part.

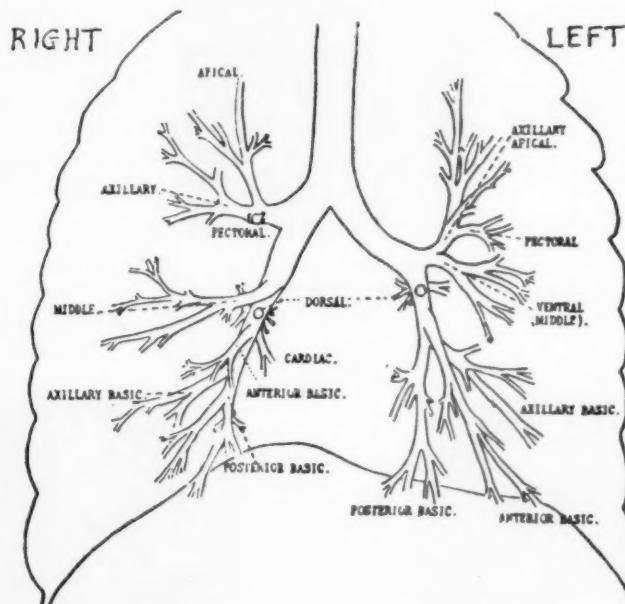


FIG. 1.—Diagram of the anatomical relation of the bronchi, prepared by the late Mr. H. P. Nelson, and reproduced from the Brompton Hospital Reports, vol. iii, 1934.

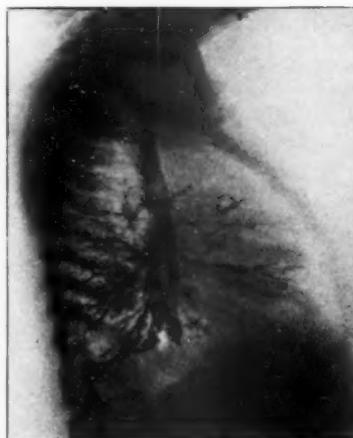
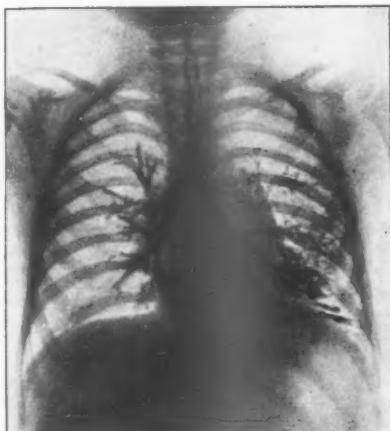
The help of radiology is needed at the present time towards solving three main problems : (1) The nature of the intrathoracic lesion ; (2) its exact anatomical distribution ; (3) the changes which have occurred following treatment.

One can claim that radiology has not only rendered possible an accurate forecast of the pathological lesion present, but has, in many instances, thrown new light on the way in which the disease originates, spreads or retrogresses during life.

The means now at our disposal for the accurate diagnosis and localization of lung disease are very different from those which were available to our predecessors to whom we owe so much, for it is they—and particularly our late friend and colleague Dr. Stanley Melville—who have taught us how to interpret the shadows which we see.

These additional methods of examination include bronchography, introduced in 1925, and tomography and kymography, introduced more recently.

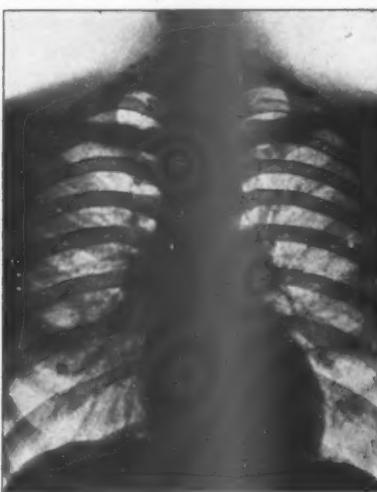
**Routine films.**—The plain routine examination must always be complete and thorough, and include, in most cases, anterior, oblique, and true lateral views, and



(a)

(b)

FIG. 2, *a* and *b*.—Female, aged 2. (Dr. Davidson's case.) Showing bronchial dilatation in the left lower lobe, and of the lingular process of the upper lobe; also showing displacement of the left upper bronchus following the atelectasis.



(a)



(b)

FIG. 3, *a* and *b* (Dr. F. H. Young's case).—Tuberculous lesion in right lower lobe, showing cavity visualized by tomography, taken at St. Bartholomew's Hospital by Dr. Meyer.

perhaps, in addition, views taken with greater penetration in the horizontal and vertical positions. Stereoscopic views may also be helpful.

To a surgeon, a report of an opacity in the right mid-zone is useless, for he will want to know its lobar distribution within the affected lobe, and its depth from the pleural surface.

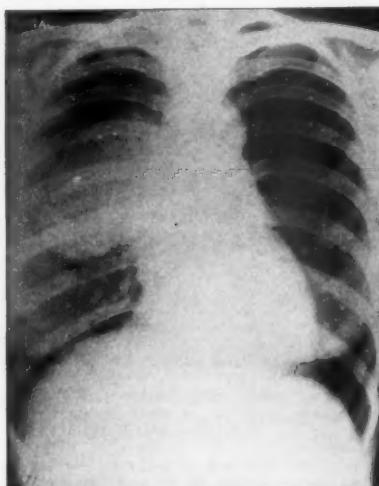


(a)



(b)

FIG. 4, *a* and *b*.—Male, aged 45. (Case under the care of Dr. Hoyle and Dr. Maxwell.) Mediastinal mass showing rapid increase in size. At the first examination, when the opacity was small, the differentiation from aortic aneurysm was difficult. The subsequent rapid increase in size of the mass and the absence of aortic pulsations in it, as seen in the kymograph, pointed to the diagnosis of mediastinal neoplasm, subsequently found. Kymograph taken by Dr. Simon.



(a)



(b)

FIG. 5, *a* and *b*.—Female, aged 45. (The late Dr. Scott Pinchin's case.) Anterior mediastinal mass, suggesting diagnosis of dermoid cyst. At operation the mass was found to be due to an aneurysm of the ascending aorta.

*Lipiodol.*—As an aid to diagnosis, lipiodol or neohydriol is frequently employed to outline the bronchial tree, and one is constantly reminded how important is the technique of these injections in order to obtain the information required.

In cases of bronchiectasis it may be necessary to repeat the injection to ascertain the exact extent of the lung involvement, for it must be realized that the surgeon is dependent on radiology alone for this information. One must also bear in mind to what a great extent the normal anatomical position of the lobes may change as a result of atelectasis or emphysema.

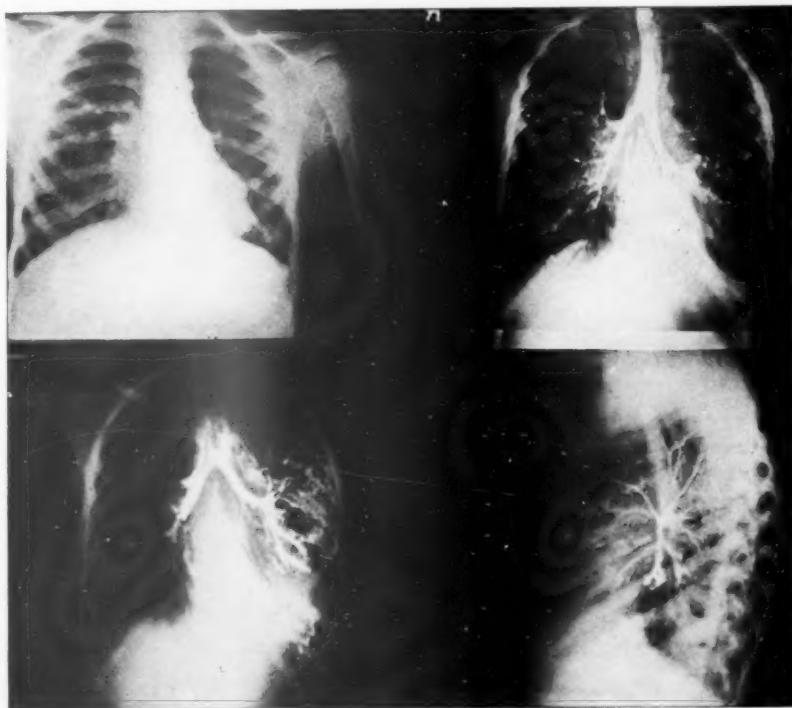


FIG. 6.—Male, aged 7. Atelectasis of left lower lobe. Bronchography fails to outline the lingular process. After lobectomy, by Mr. Roberts, residual dilatation is seen in the lingular process.

In this connexion, it is the middle lobe on the right side, or the corresponding lingular process on the left side which may be left when subsequent radiographs show gross dilatation in their bronchi.

It has been found preferable to examine each lung individually so as to avoid overlapping shadows in the lateral view, the patient being rotated forwards during the injection to ensure a filling of the middle lobe area. Views should be taken with the patient lying as well as erect, and there should be no hesitation to repeat an opaque injection after a suitable interval if it does not give all the information required.

*Tomography.*—The tomographic examination of the chest has come more recently to the fore as a means of accurate localization of lung disease, by taking radiograms

of the chest in layers. I shall not enlarge on this subject to-night, except to say that owing to the ingenuity of Dr. Twining we have been able to add a tomographic attachment to our existing apparatus at a cost of less than £2.

By this means we have been enabled to demonstrate cavities unsuspected in the plain film, and to render more clearly visible those which were previously suspected. And we are also able to tell the exact depth at which each cavity is lying.

*Kymography.*—This more neglected new method of examination it may seem out of place to mention as an aid to diagnosis in surgical cases, but I have had two cases in which it would, I believe, have enabled us to arrive at an accurate diagnosis; in one of these the patient died subsequently, after a thoracotomy.

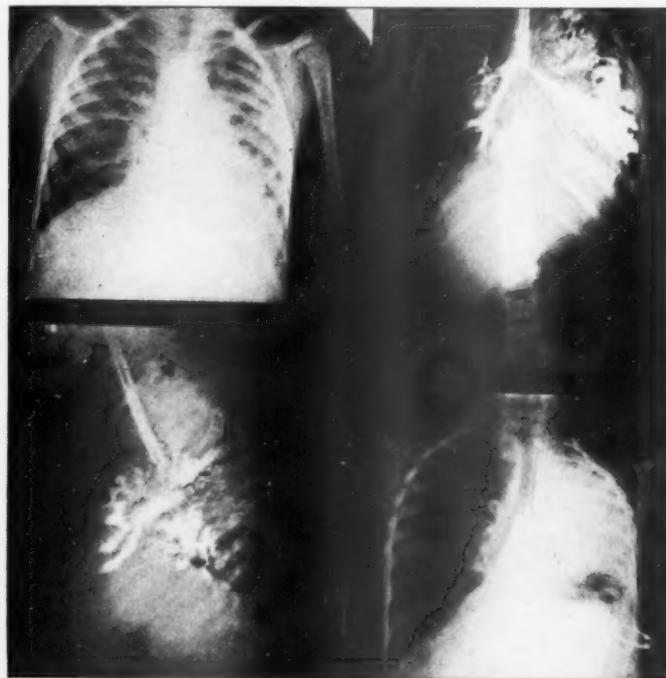


FIG. 7.—Male, aged 5. Bronchiectasis in all zones of left lung, before and after bronchography. The right lower reproduction shows appearances after total pneumonectomy, by Mr. Roberts, and after phrenic avulsion. The wound is now healed.

*Bronchiectasis.*—What, then, can radiology tell us with regard to bronchiectasis?

Firstly, it can tell us if the patient *has* bronchiectasis—a condition infrequently correctly diagnosed before the use of X-rays, and secondly, it can tell us the type of bronchial dilatation, and its extent and distribution.

The advent of lobectomy and pneumonectomy as surgical possibilities is probably the greatest advance in modern surgery, offering the possibility of cure to cases of bronchiectasis whose lives might otherwise have remained a constant source of distress both to themselves and to others associated with them.

Lobectomy does not, however, render obsolete other forms of treatment, such as medical treatment and postural drainage, advocated by the late Mr. H. P. Nelson.

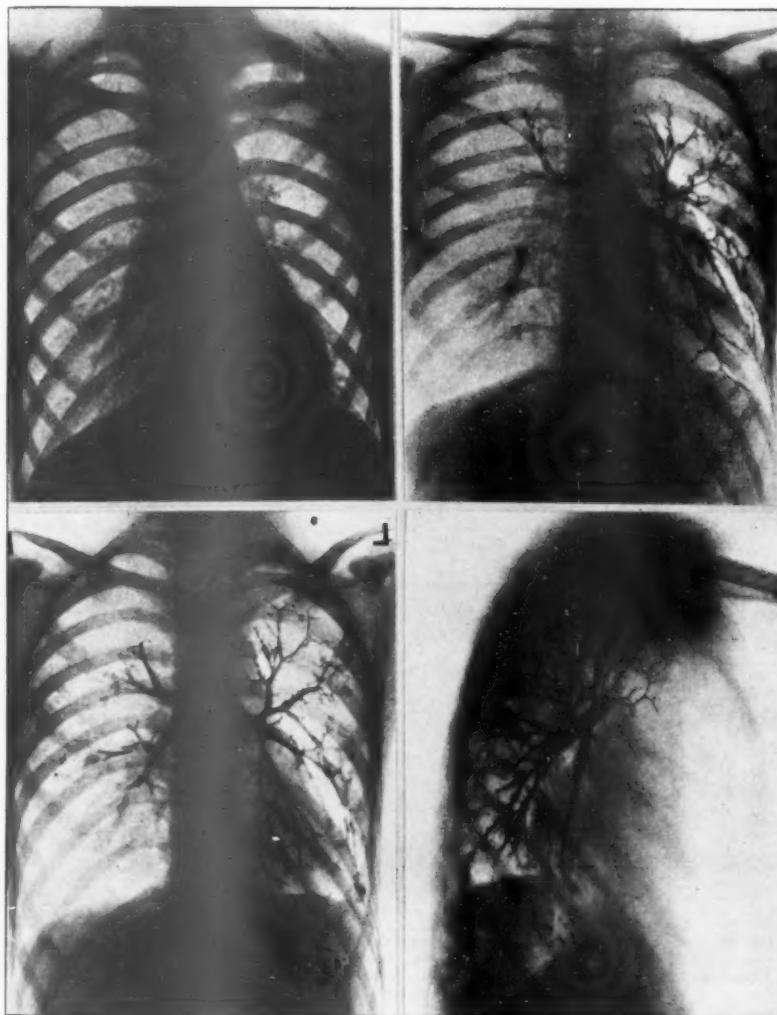


FIG. 8.—Male, aged 15. Had suffered since childhood with attacks of bronchitis and bronchospasm. History of five attacks of "pneumonia". The preliminary radiogram shows atelectasis of the left lower lobe. After bronchography, dilatations are seen in this lobe, and a peculiar fusiform appearance is seen in one or two of the upper bronchi on both sides. He had, on occasions, brought up 4 to 5 oz. of frothy sputum. The comparative bronchograms were taken eight months after a left lower lobectomy by Mr. Brock. Note the posterior position of the bronchi of the lingular process after lobectomy.

In fact a prolonged course of such treatment is often necessary and desirable to get the patient into a fit state to withstand the operation.

Lobectomy has, however, rendered less desirable various forms of collapse-therapy previously practised, and often found to be palliative, but not curative. Such methods as phrenic avulsion, thoracoplasty, and artificial pneumothorax have, therefore, taken a second place—phrenic avulsion because it is one of the contraindications to subsequent lobectomy, and thoracoplasty because, though alleviating symptoms in some cases, it does not obliterate or compress the septic cavities. Artificial pneumothorax is still used in certain cases to diminish the amount of

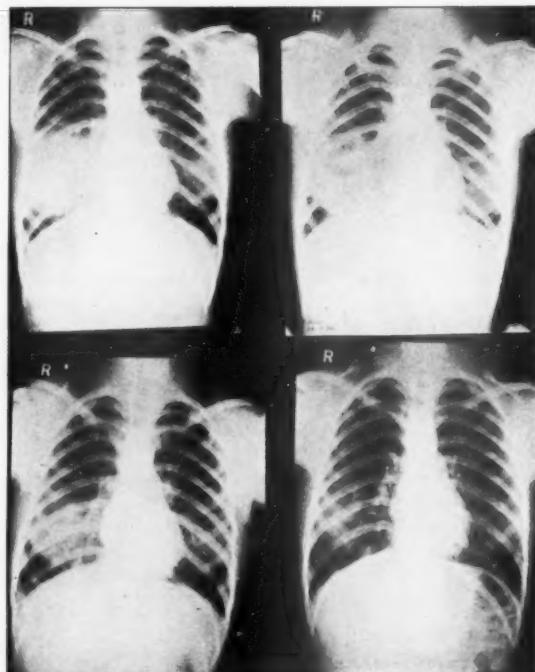


FIG. 9.—Patient, aged 12. (Dr. F. H. Young's case.) Cough for two weeks and no sputum. A lung abscess is seen spreading and excavating in the lung. Treatment by rest and postural drainage produced rapid clearing of the inflammatory lesion. A subsequent bronchogram showed a normal bronchial tree.

sputum, previous to surgical removal of a lobe, but should not be continued indefinitely, lest thickening of the visceral pleura should impede lobar expansion after lobectomy.

*Lung abscess.*—Radiology is employed in cases of lung abscess, firstly to verify the presence of such a lesion, and secondly to localize its position and extent. In some cases lipiodol may fail to enter the abscess cavity, leaving the area "silent".

Tomography may also prove invaluable in demonstrating the presence of cavitation—or of more than one cavity in the involved area—and in localizing accurately the depth of the lesion.

Postural drainage is again frequently employed in treatment and the progress of the lesion can be noted by subsequent radiographs.

In some cases in which surgical drainage is indicated it is also important to skin-mark the exact location of the abscess cavity before operation, with the patient's arm in a position similar to that in which it will be placed on the operating table. In this way failure to locate the abscess cavity is frequently obviated.

I show here illustrations of three different types of lung abscess. The first has no well-defined borders and multiple cavities; it disappeared spontaneously with postural drainage, showing subsequently a normal bronchogram.

The second was moderately localized and contained a fluid level simulating,

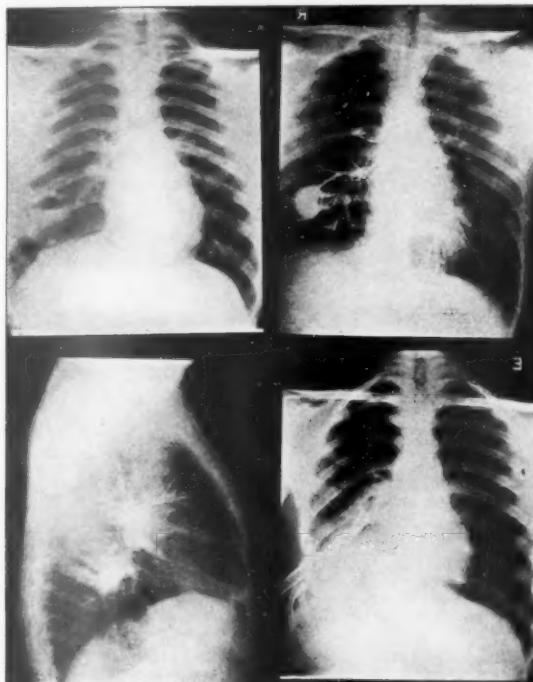


FIG. 10.—Male, aged 21. Symptoms had persisted for eight months. Abscess simulates a tuberculous cavity. Lipiodol shows free entry, suggesting epithelialization of the abscess cavity. Subsequently bronchiectasis developed around the abscess, and a lobectomy was performed by Mr. Price Thomas. The patient is now back at work as a collier.

radiologically, a tuberculous cavity. It allowed free entry of lipiodol and was subsequently treated by lobectomy, owing to the associated bronchiectasis.

The third shows a very sharply defined margin simulating a neoplasm, and containing a fluid level. In this case the abscess was drained surgically.

*Tuberculosis.*—Surgical treatment in tuberculosis is mainly directed to assist in effecting pulmonary compression or collapse. Here radiology plays an important part, in demonstrating the presence and position of cavity formation, but gives no indication as to whether such cavity should be treated by surgical means.

Serial radiography does certainly indicate how long a cavity may have been present, and any changes in its size can be recorded when accurate technique is employed. Radiology may also give some indication of the nature of the wall of such a cavity and show whether the cavity contains secretion or not.

The serial radiographic examination, though not indicating the particular line of treatment to be employed, may give the clinician some indication of the effect of previous treatment in controlling the lesion and, in conjunction with other clinical data, it may help in deciding which type of treatment is possible.

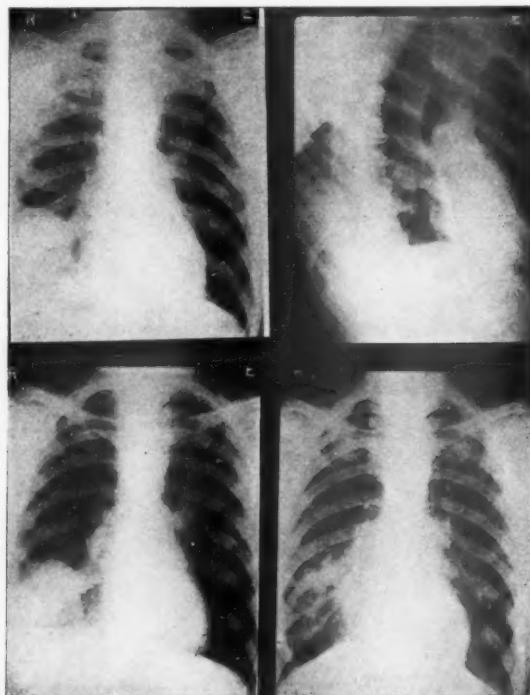


FIG. 11.—Male, aged 40, a deep-sea diver. (Dr. Burrell's case.) Severe cough; 2 to 6 oz. of purulent sputum. This patient had previously had tuberculosis of the lungs in 1934. The abscess, which is draining freely, has sharply defined borders, and simulates a neoplasm radiographically. The abscess was drained by Mr. Brock. The patient is now well.

Burrell, in a recent communication, stresses the importance of treating the disease rather than the cavitation, and emphasizes that active measures to close a cavity of the dry fibrotic type may often aggravate the disease and shorten life.

Fortunately many cavities diminish in size with rest, and some can definitely be seen to disappear. In other cases, however, cavities may remain stationary or even become larger, whilst in others fresh areas of disease or cavitation may appear.

The treatment will, of course, vary with each individual case, depending largely

on the skill and experience of the physician and surgeon ; and an increasing number of cases are now receiving surgical aid.

Among the methods of collapse are artificial pneumothorax, phrenic crush, phrenic avulsion, adhesiotomy, apicolysis, extrapleural pneumothorax, and thoracoplasty—each of which may play an important part in bringing about effective rest or compression to the affected portion of the lung at the proper time.

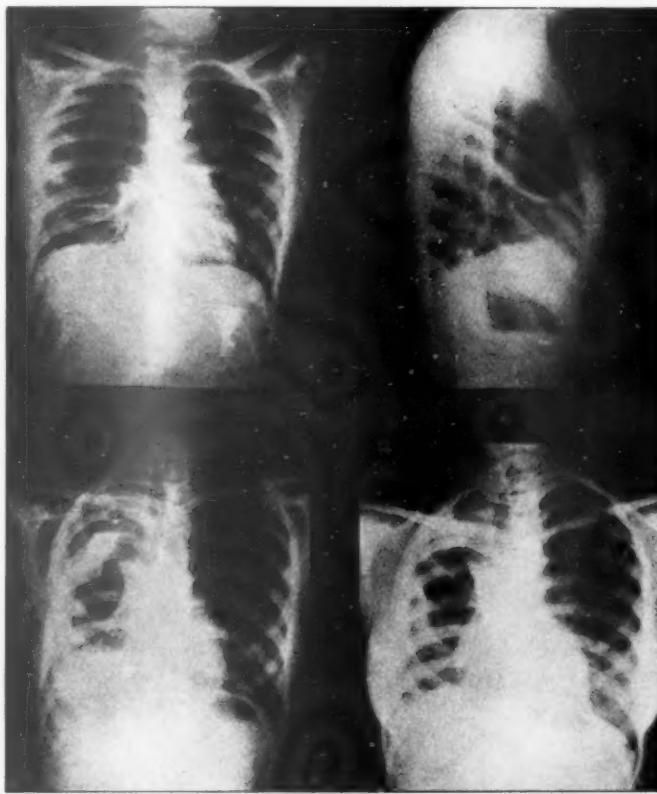


FIG. 12.—Female, aged 10. Complained of persistent cough, so severe that she had to sleep in the prone position ; she could not lie supine without bringing on a spasm of coughing. The radiograms show a large translucent cavity in the right field, containing a fluid level and suggesting a cyst. The lipiodol, in this case, showed the opaque material passing into the pleura. Upper-lobe lobectomy was performed by Mr. Tudor Edwards, and a large cyst was found and removed. The upper two reproductions show the cyst before operation ; the left lower reproduction shows an injection of the residual sinus ; and the right lower reproduction shows the appearance now that the sinus has healed. The patient is now well.

*Conclusion.*—It has been my privilege to-night to show you a few of the surgical successes of my colleagues in which radiology has played its part, and I should like to take this opportunity of congratulating them on the remarkable results obtained.

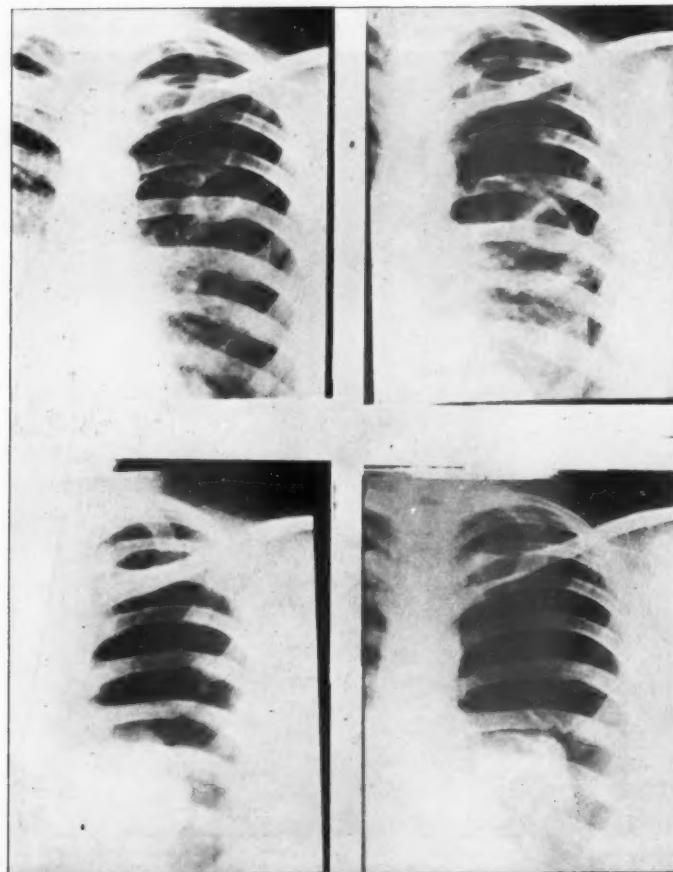


FIG. 13.—Female, aged 23. (Dr. Marshall's case.) Cavity healing after adhesiotomy by Mr. Price Thomas.

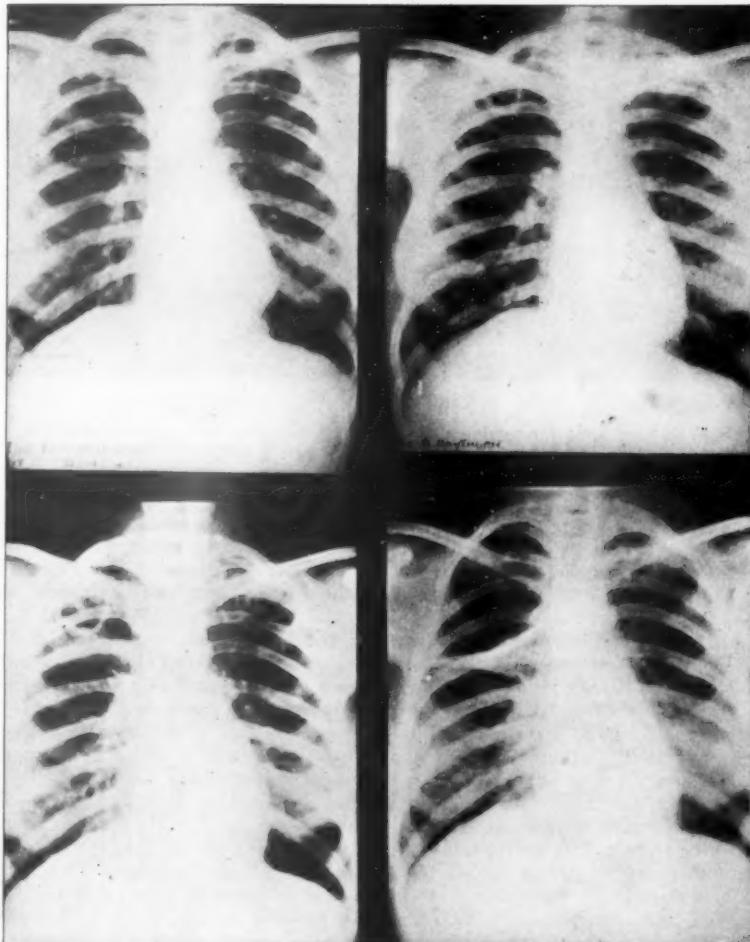


FIG. 14.—Adult female, under the care of Dr. Todd at the Midhurst Sanatorium. Cavity increasing in size under sanatorium treatment. Extrapleural pneumothorax, performed by Mr. Tudor Edwards, showing remarkable compression of the upper zone, with healing of the lesion in the opposite apex, following operation.

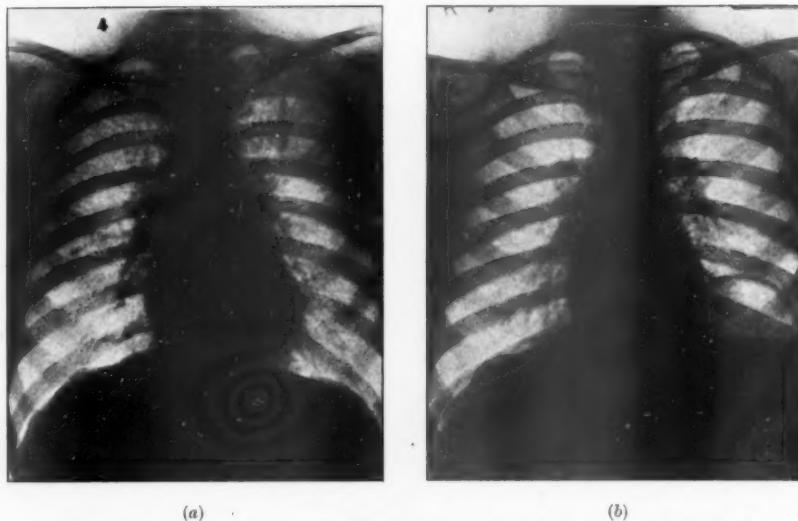


FIG. 15, *a* and *b*.—Adult male. (Dr. Lloyd's case.) Large cavity in the left upper lobe, where pneumothorax was attempted and failed. Later phrenic avulsion was performed by Mr. Price Thomas, and at present the cavity cannot be recognized in the plain X-ray film.

**Dr. E. W. Twining:** *Neoplastic lesions.*—The subject allotted to me in this discussion is a very large one. It was discussed *in extenso* at a meeting of the Section of Surgery, February 5, 1930, and the report filled 13 pages of the *Proceedings*, 1930, 23, 689 (Sect. Surg., 25). Since then there have been many valuable contributions to the literature.

I am chiefly concerned this evening with the benign tumours—and it must be emphasized at the outset that they are relatively rare. A radiologist may expect to see a malignant lung lesion about once a week; he will probably not see a benign lung tumour more often than three or four times a year. The common criterion of a benign tumour—smoothness and definition of outline—is in reality of little diagnostic value. Malignant tumours of the mediastinum will retain a smooth, well-defined border so long as they are confined by the mediastinal pleura, and this barrier to direct spread is maintained for a very long time. I do not recollect any case in which a malignant tumour arising in the mediastinum proper has directly invaded the lung by breaking through the mediastinal and visceral pleural barrier. In my experience such invasion always occurs by way of the hilum. An appearance of a hairy edge, sometimes mistaken for direct infiltration, is due to pressure upon, and congestion of the veins, and it disappears, if the mass is reduced in size, by radiotherapy. A similar hairy edge, due to the same cause, may be seen in cases of large aneurysm. Mediastinal tumours, having an appearance resembling that of a benign tumour, are often lymphadenomatous. Typically, they have a lobulated contour, the lobulations being due to enlargement of specific groups of glands (paratracheal, tracheobronchial, or aortic, &c.) which can be recognized radiologically. But secondary malignancy, from carcinoma of the lung itself, or of any situation outside the lung, or secondary *sarcoma*, may also produce well-defined smooth or lobulated mediastinal masses which may be unilateral or bilateral. Primary mediastinal lymphosarcoma, once thought to be a common mediastinal tumour, is actually very rare.

Such mediastinal tumours are seldom subjected to surgery, in the belief that they are benign, but instances of this mistake are reported from time to time in the literature, as is the case of a fatal surgical intervention in a case of lymphadenoma of the mediastinum reported by Leriche.

In the lung field, well-defined rounded tumours are far more likely to be malignant than benign. The commonest cause of an isolated rounded lung shadow is a solitary metastasis. The next in order of frequency is a primary lung carcinoma arising from a small peripheral bronchus. If such a tumour is found, an early lobectomy may be successful. Even a solitary metastasis may be successfully removed, as instanced by a case reported by Mr. Tudor Edwards ; in this case the patient is still alive after a long period since the operation.

It is therefore unwise to temporize in such cases, and the second radiological criterion of benign tumour of the lung—slow rate of growth—loses its importance, for we cannot safely wait for re-examination. The case should be brought to the notice of the surgeon at an early date. An isolated peripheral carcinoma may, in the course of one or two months, spread by the lymphatics to the hilum, and show a band of shadow connecting it with the hilum ; at this stage the most favourable moment for intervention has passed.

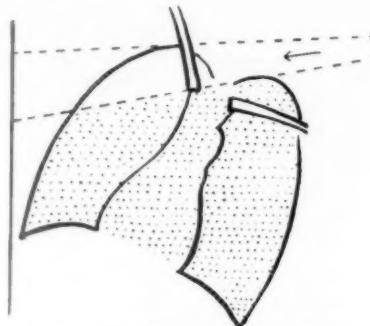


FIG. 1.—Oblique lateral projection of apex.

The subsequent investigation of the case involves the use of diagnostic measures, not exclusively radiological (artificial pneumothorax, lipiodol, bronchoscopy, serological tests, thoracoscopy, &c.). Radiology alone cannot be depended upon for a diagnosis. Even when all diagnostic measures have been exhausted, surgeons admit freely that they sometimes have to perform a thoracotomy without a definite diagnosis. Radiologists may safely imitate this frankness, and admit that their diagnosis can at best be merely provisional. But though a surgeon may have to enter the chest without a foreknowledge of the nature of the lesion, he will never do so without knowing the site accurately.

Localization, therefore, is of even greater moment than diagnosis. I will not dwell here upon the familiar routine measures of localization. I believe that the guild of radiological magicians who make a diagnosis and localization from a single antero-posterior film is rapidly dying out—the art is all but lost ; the rest of us find radiography and screening in many planes essential. In more than half the cases a routine "postero-anterior and lateral" gives the essential information. But these standard views only, must be insufficient. If a tumour is in the apical region of the lung, an oblique interclavicular lateral projection, which I have described elsewhere, is sometimes of distinct value. The ray enters the opposite supraclavicular region, and emerges through the axilla of the side to be examined (fig. 1). In the case of

bronchostenosis and lower lobe collapse, also, the lateral view is often insufficient, when the interlobar fissure has rotated backwards and the collapsed lower lobe lies in the paravertebral region. The fissure then faces neither directly forwards, nor directly laterally, and an oblique projection is necessary to show the well-defined edge of the collapsed lobe (fig. 2).

In describing the position of a neoplasm I do not use the term "zone". Usually we can assign the lesion to a definite segment of a lobe, and define its relation to pleura, chest wall, and mediastinum.

An exact knowledge of the anatomy of the lobes, of their position in the healthy chest, and the variations of their position in the normal chest, is an essential part of radiological equipment. Not only so, but the bronchial and vascular supply of each lobe segment must be known in considerable detail.

*Solitary rounded shadows in the lung.*—There are four common causes of isolated rounded shadows in the lung field.

These are, in order of frequency : (1) A solitary metastasis. (2) Primary carcinoma of a peripheral bronchus. (3) Encysted interlobar effusion. (4) Hydatid cyst.

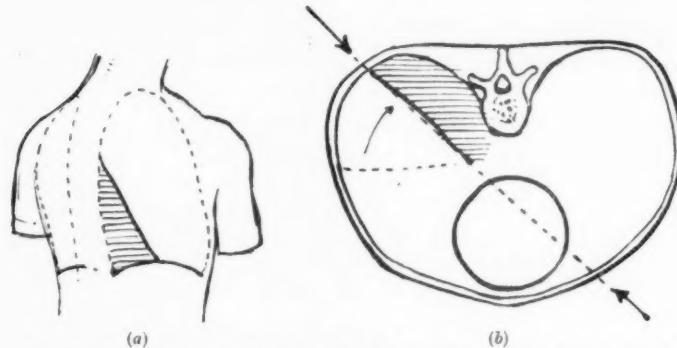


FIG. 2.—(a) Oblique projection for collapsed lower lobe, where it has rotated into paravertebral region. (b) Collapsed lower lobe, with rotation of the interlobe. Dotted line gives the direction of ray necessary to show the edge of the lobe.

In addition there are numerous rare rounded shadows which may simulate a benign tumour or in some cases be caused by benign tumour.

(1) Tuberculous : (a) Rounded "Assmann's focus". (b) Tuberculoma, sometimes calcified. (c) Ghon's focus.

(2) Other inflammatory lesions : (a) Pneumonitis (abscess, pneumonia, &c.). (b) Gumma. (c) Actinomycosis.

(3) Cysts : (a) Fluid filled bronchial cyst. (b) Lymphangiectatic cyst.

(4) Vascular lesions : (a) Infarct. (b) Pulmonary aneurysm. (c) Dilated pulmonary vein. (d) Thrombophlebitis migrans.

(5) Tumour, benign : (a) Chondroma. (b) Fibroma.

(6) Tumour, malignant : Primary sarcoma.

*Mediastinal tumours.*—Primary mediastinal tumours may arise in various tissues :

(1) From lymphatic glands : Lymphadenoma, lymphosarcoma, lymphoma (leukaemia), from lymphatic vessels, lymphangiomatous cyst.

(2) From the thyroid gland : Substernal thyroid—simple or malignant.

(3) From the thymus : Simple hyperplasia, thymic cyst, thymic tumour (thymoma, carcinoma, sarcoma).

- (4) From connective tissue : Lipoma, fibroma, xanthoma, chondroma, chondrosarcoma, and sarcoma.
- (5) From pleura : Endothelioma.
- (6) From the pericardium : Pericardial cyst, pericardial diverticulum.
- (7) From nerve tissue : Ganglioneuroma, neurofibroma, "hour-glass tumour", neuroblastoma.
- (8) From embryonic elements : (a) Vestigial : Tracheobronchial cyst, oesophageal cyst. (b) Dermoid and teratoma.

*Substernal thyroid.*—Substernal thyroid is usually a downward projection of a cervical goitre, but may develop within the thorax, with no obvious thyroid enlargement in the neck. During old age, an old-standing adenoma may gradually disappear from the neck, and be found retrosternally, apparently as a result of increasing kyphosis.

Radiologically, a substernal thyroid is usually seen as a somewhat pyramidal shadow continued upwards into the neck, moving upwards on swallowing, unless malignant or adherent. The trachea is compressed, and the narrowing can be traced upwards into the neck, a point of distinction from the majority of true mediastinal tumours. Very often the enlargement is unilateral and the trachea displaced towards the opposite side. In the lateral view the trachea may be displaced backwards, and show a broad indentation of its anterior margin. If the tumour has developed retrosternally, anterior displacement of the trachea is found. The oesophagus is displaced backwards or laterally. The aortic knob may be displaced downwards if the tumour is large. Calcification may be visible in the substernal thyroid—if in the capsule, in the form of a dense line covering its surface; more commonly the calcification is scattered in the form of flecks through the substance of the tumour. A very large unilateral substernal thyroid may completely fill the apical region of one lung, and present an appearance indistinguishable from that of a large neurofibroma.

*Tumours of the thymus.*—Primary thymic tumours are rare. Decker (1935) has collected 208 recorded cases. Since then they have been reported at the rate of about two a year. Three types are described : (a) Malignant thymoma or lymphosarcoma composed of round or polyhedral cells, with islands of cells of epithelial type. Some show a structure reminiscent of the "lymphepithelioma" of the fauces and pharynx. (b) Carcinoma, supposedly derived from cells of Hassall's corpuscles. (c) Sarcoma arising from the stroma. (d) Simple dermoid cysts and ciliated cysts, arising from the thymus anlage, have been described.

Clinically, malignant thymic tumours produce local pressure symptoms at the thoracic inlet. They metastasize to glands of the neck or axilla or elsewhere, and tend to penetrate the capsule of the gland and invade local structures. The sternum may be eroded, and in a case which I recently saw (fig. 3), the tumour had infiltrated widely into the mediastinum and neck, and had perforated the trachea. Symptoms of myasthenia gravis may be associated with thymus tumour.

Radiographically, thymomata are difficult to distinguish from other malignant mediastinal tumours. They occupy the anterior mediastinum, in the retrosternal space, and are usually lower in position than other mediastinal tumours, broader than they are long, and springing boldly outwards into the lung field. This projection is more often bilateral than unilateral. The outline is well defined and may be lobulated. The trachea is usually compressed or displaced laterally.

Thymoma is radiosensitive, and in some cases the patients have survived for periods of 3-6 years after X-ray treatment. The carcinomata are not radiosensitive. Fig. 3 illustrates a case of thymoma.

**Case I.** The patient complained of difficulty in breathing and of loss of voice. The tumour began, in 1933, with a swelling above the right clavicle. This was excised and the area was treated by X-rays. The patient was free from symptoms for eighteen months after treatment; then he began to have a constant cough and gradual loss of voice. He was admitted to hospital in January 1936 and a mediastinal abscess was diagnosed. He had no sputum or haemoptysis and no difficulty in swallowing.

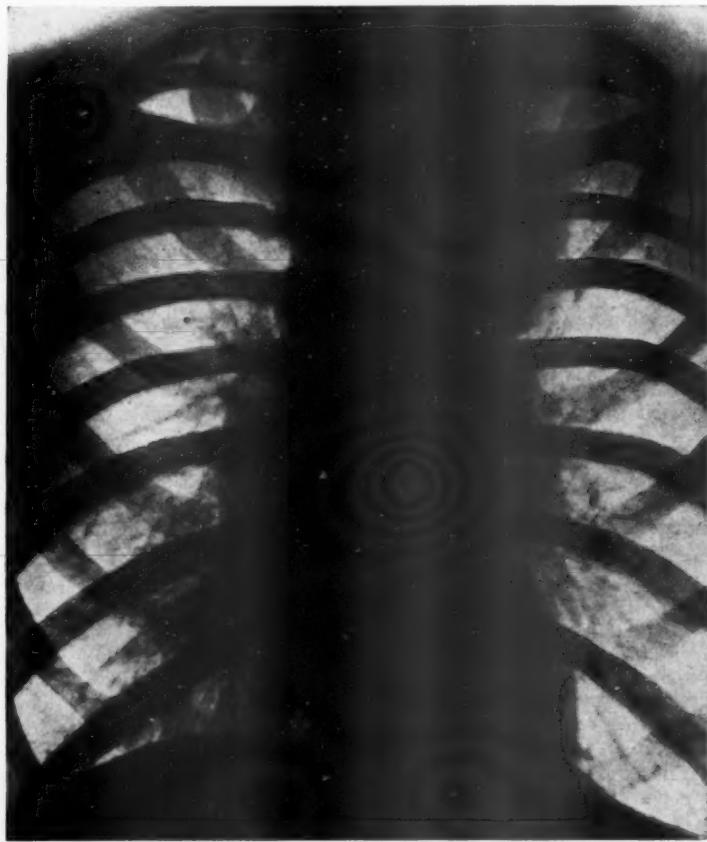


FIG. 3a (Case I).—Thymoma.

First radiological report: "Opacity under manubrium sterni suggesting enlarged retrosternal thyroid. The shadow projects more to the left than to the right. The oesophagus is not displaced or compressed, but the trachea appears to be compressed above the sternal notch."

The patient died, and post-mortem findings were as follows: In the right lower lobe there were areas of consolidation—many haemorrhagic—and several enlarged hilum glands (secondary growth). The left lung was somewhat congested; one large gland in the hilum was secondarily invaded. The trachea was extensively congested; the right side, below the cricoid, was compressed from the lateral aspect, a large mass of growth almost surrounding

it. In this region invasion of mucosa had occurred; several nodules of growth were visible. The bronchi were intensely congested and contained much pus.

*Thymus*.—The site of the thymus is occupied by a large mass of very firm, yellowish white growth, which is adherent anteriorly to the sternum, extends around the trachea and well into the anterior triangles of the neck on both sides, almost to the angles of the jaws; the latter masses appear to be glands enlarged by secondary invasion. The growth has compressed the trachea, mainly from the lateral aspects. The thyroid gland has been invaded at the

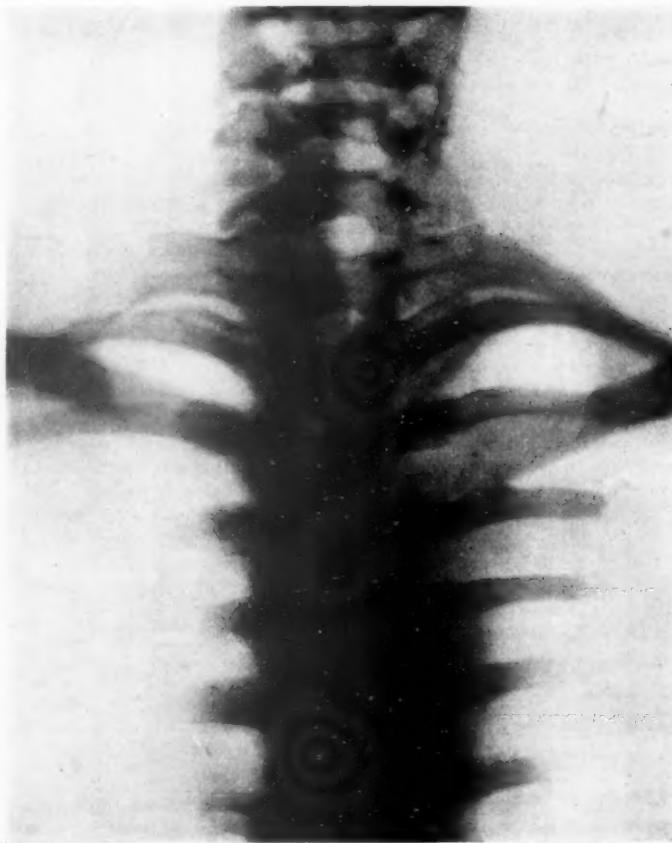


FIG. 3b (Case I).—Thymoma. Penetrating film showing compression of the trachea.

lower poles; the great vessels of the neck have been completely surrounded by the growth. Secondary growths were present in the glands at the bifurcation of the trachea and in the tracheobronchial glands of both sides. No other secondaries were found and there was no indication of a primary tumour in the lungs.

Microscopical examination showed the tumour to be composed mainly of masses of medium-sized round cells among which were varying numbers of larger cells; a considerable amount of fibrous tissue was present, dividing the tumour into foci of varying size. The features were those of a malignant thymoma.

*Dermoid cysts and teratomata.*—The pathology of these congenital tumours is obscure and their origin disputed. Hedblom has classified them according to their histology. Those which contain ectodermal derivatives only, he classifies as epidermoids; if all three layers are represented they are teratomata. For practical purposes they are most conveniently classed together as dermoids. Most of them are cystic; some are solid, or partly solid and partly cystic. They contain hair, oily or sebaceous material, cholesterolin and, occasionally, bone or teeth. In old-standing cases the walls may calcify. Though they are nearly always benign, malignant degeneration has been known to occur in just under 10% of all cases, and may lead to rapid increase in size. Clinically males and females are affected in nearly equal numbers.

Symptoms: Pain, irritating cough, haemoptysis, or signs of pressure, usually occur in early life—before the age of 30 years. There is often a rapid increase in size at puberty.

If the cyst perforates into a bronchus, hair, or oily contents may be expectorated. Infection may follow, and perforation into the pleural cavity; several hitherto unsuspected dermoids have been encountered during operation for empyema.

Chorionic tissue is sometimes present, testicular atrophy or gynecomastia may coexist, and the Aschheim-Zondek test may be positive.

Radiologically they present the following features:—

(1) Position: This is variable. Usually it is below the level of the aortic arch, though in a few cases the cyst has occurred in the upper mediastinum, obscuring the aortic arch and simulating aortic aneurysm, a substernal thyroid or thymus tumour. Duval has classified them, according to position, into four groups, viz.: (i) Retrosternal, between the mediastinal pleura and the sternum. (ii) Cervico-retrosternal, presenting in the sternal notch. (iii) Mediastino-thoracic, extending from the mediastinum into one thoracic cavity. (iv) Lateral thoracic, lying almost entirely in one thoracic cavity.

In nearly all cases they are anterior. In three cases out of 185 reviewed by Hedblom, the tumour lay in the posterior mediastinum and in one case (Jagger) it lay in contact with the posterior chest wall and communicated through an intercostal space with an external fatty swelling. Only in extremely rare cases is the tumour separated from the mediastinum. In one case it apparently took origin from the diaphragm (Harrington).

(2) Contents: Teeth, or bony particles, may be observed radiologically. In one unique case, observed by Phemister, and confirmed by operation, the fatty contents, fluid at body temperature, separated out from the more fluid contents, upon which they floated. This produced a horizontal fluid level, surmounted by a more translucent zone, resembling an air bubble but of greater density, due to the fatty layer; from this the nature of the cyst was correctly deduced.

Teratomata: The more fleshy teratomata, containing no cysts, or relatively small single or multiple cysts, usually show smoothly contoured circular outlines. Hammarström has described in two cases a slightly wavy or lobulated outline, due to different rates of growth of various tissues composing the tumour, which he suggests may distinguish them from thinner-walled cysts.

The differential diagnosis is from encysted empyema, aortic aneurysm, encysted effusion, hydatid cyst, substernal thyroid, thymus tumour, paravertebral abscess, bronchogenic carcinoma, mediastinal tumour, lymphosarcoma, lymphadenoma, or other enlargements of the lymphatic nodes, fibroma, and lipoma.

*Case II. Dermoid cyst (fig. 4, a and b).*—A. H., female, aged 7. During routine X-ray examination of the chest after an attack of measles followed for two years by attacks of malaise and pyrexia, a large mass was found in the left side of the chest. It projected far

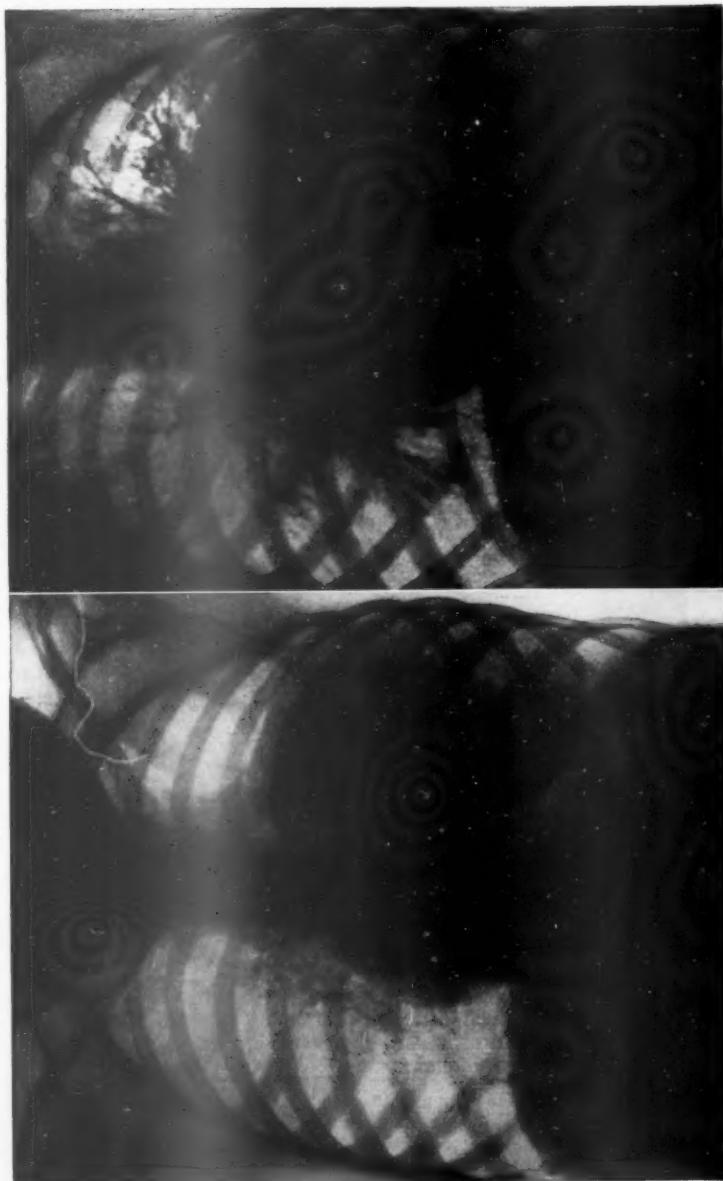


FIG. 4 (Case II).—(a) Dermoid cyst. (b) The same : Showing lipiodol-filled bronchi, displaced inwards and backwards.  
(a)  
(b)

down into the lung field, reaching the diaphragm; its upper pole fused with the mediastinal shadow. A few dense particles were seen within it on which a diagnosis of probable dermoid containing tooth or bone were made. In the full lateral view it lay at about mid-depth in the chest, and on lipiodol examination in the postero-anterior view the bronchi were found to be festooned around the tumour, and in the oblique view the clear-cut posterior margin of the tumour was beautifully outlined by the bronchi. The tumour was successfully removed by Mr. Graham Bryce. It was a large dermoid cyst and it contained fragments of dental tissue and sebaceous material. It was extrapulmonary. It arose from the superior mediastinum by a pedicle as thick as the thumb and was partly adherent to the thymus and pericardium. The patient made a good recovery and was quite well within three months.

It is obvious that such a case might easily be mistaken for chronic interlobar empyema which, if old-standing, may form a large round shadow. As a rule, the interlobar empyema of this type is better defined on its lower than on its upper margin, because the weight of the fluid accumulating in the lower pole makes this more

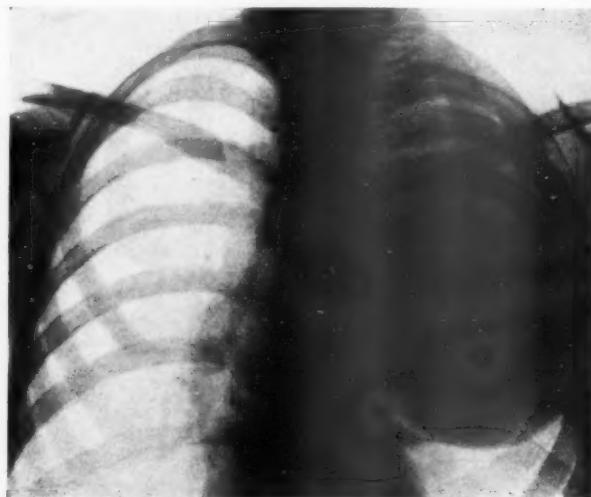


FIG. 5 (Case III).—Interlobar empyema.

truly circular. Also in the anterior view a large interlobar effusion in the main fissure tends to be hatchet-shaped, i.e. approximating to a triangle, with its apex pointing to the hilum and at hilum level. Since, however, a dermoid may extend outwards in an interlobar fissure, and even a hydatid cyst may develop within an interlobar fissure, as related by Fleischner, the differential diagnosis must sometimes be a matter of extreme difficulty. How closely a chronic interlobar empyema may approximate to the cystic form is shown by the following case:—

*Case III* (fig. 5).—Patient, female aged 19, was for four years detained in a sanatorium, without X-ray examination, as a suspected case of tuberculosis. Her private doctor at the end of this time found some apical dullness on percussion. X-ray examination at the Royal Infirmary showed a large, almost globular, shadow in the lung which was diagnosed as an interlobar empyema. At operation Professor Telford found an interlobar empyema containing pus, which gave a pure pneumococcal culture. The patient made a good recovery.

A dermoid usually projects to one side and it is stated that it does not displace the heart. In the anterior mediastinum it may, however, project to both sides and displace the heart downwards and backwards.

Calcification in the wall of a dermoid cyst is exemplified in the following case, for which I am indebted to Dr. M. H. Jupe :—

*Case IV (fig. 6, a and b).*—Patient, male, aged 57. History of six months' bronchitis, temperature and pain in the left chest anteriorly, with dullness and diminished air entry. Tests for hydatid cysts negative. The X-ray showed a large, well-defined shadow with definite calcification along the margin in the left lung field projecting from the mediastinum.

Lipiodol filled the lower lobe bronchi, and one upper lobe bronchus can be seen in the lateral view running round the posterior margin of the tumour, evidently displaced backwards from its normal position. Diagnosis of dermoid cyst was made and it was removed. It was found to be adherent to the innominate vein and pulmonary artery.

*Lipoma and fibroma* of the mediastinum, excluding neurofibromata, are very rare. Twenty cases of fibroma are recorded. Lipomata may arise from the fatty tissue of the anterior mediastinum. Some of them, Hammarskjöld suggests, may be unusually fatty teratomata; others grown from the posterior mediastinum. Radiologically they present as mediastinal tumours with smoothly defined or lobulated contours, and may grow to an enormous size. They occasionally grow upwards through the thoracic inlet into the neck, or are partly intra- and partly extra-thoracic, communicating by an isthmus through the sternum or an intercostal space.

It is probable that fibromata of the chest wall are usually of neurogenic origin. They are found subpleurally on the chest wall, usually posteriorly. Mixed forms occur—e.g. fibroleiomyomata, described by Jacobaeus and Key. Apart from neurogenic tumours, I have not met with a case in fifteen years.

Harrington<sup>1</sup> has published 46 cases of intrathoracic tumours removed at operation. Eleven were neurofibromata, ten of these in the posterior mediastinum and one on the thoracic wall arising from an intercostal nerve. Two were cellular fibromas in the posterior mediastinum and one was a fibromyxoma in the posterior mediastinum. Endothelioma and lipoma were also recorded by Harrington. Endothelioma, being a malignant tumour, is not likely to masquerade as a benign tumour very long. It may grow from several centres in sheath or invade the lung, and is likely to give rise to pleural effusion at an early stage.

A case of fibroma was recorded by Iles, but it is not stated whether it was neurogenic. The case published by Burrell and Melville as one of fibroma is wrongly described. The same case was described by Tudor Edwards, who removed the growth, which was a chondrosarcoma of the rib. The specimen is in the Museum of the Royal College of Surgeons.

*Neurogenic tumours.*—Neurinomata and ganglioneuromata are tumours arising from nerve tissue. These may arise from sympathetic, vagus, or intercostal nerves. They cause shadows with clearly defined contours which project from the mediastinum or the thoracic wall into the lung field.

*Neurofibroma of the vagus.*—A neurofibroma of the vagus, which underwent sarcomatous degeneration, was described by Redlich. The case has been republished by Lenk and by Assmann. The tumour occurred in a woman aged 35, and caused marked dyspnoea and cyanosis. X-ray examination showed a tumour with a crescentic well-defined outline extending along the right border of the heart, from just below the clavicle to the diaphragm. Post mortem the right vagus was found embedded in the tumour, and there were smaller tumours on both vagi and in the medulla of the right suprarenal. Subcutaneous neurofibromatosis (von Recklinghausen type) was present.

<sup>1</sup> *Journ. Thorac. Surg.*, 1934, 3, 590.

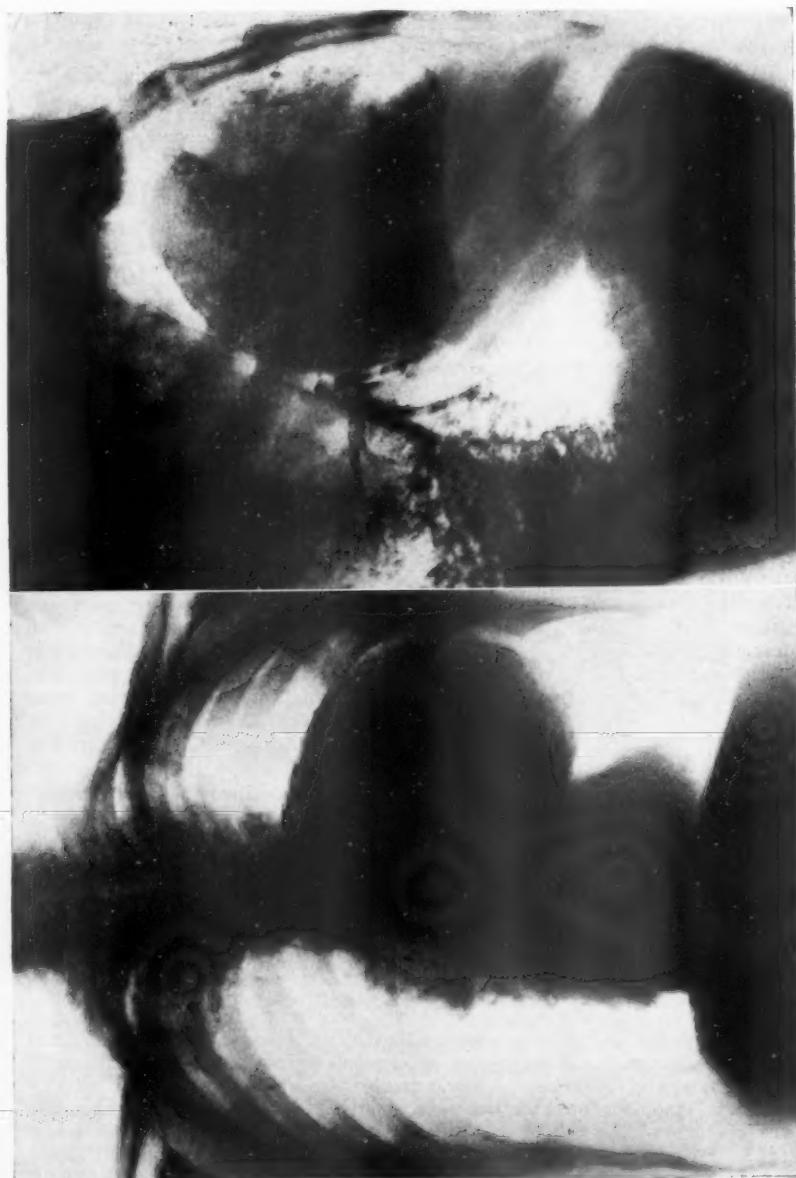


FIG. 6 (Case IV).—Dermoid cyst with calcification in the walls (Dr. M. H. Jupe's case).  
(a)  
(b)

Histologically the neurofibromas show a structure similar to that of acoustic neuroma. Palisade arrangement of the nuclei may be seen. A few have the structure of xanthoma. Malignant degeneration may occur.

Symptoms are mild or absent. When of large size, these tumours may cause dyspnoea or irritable cough from pressure on the trachea, or dysphagia by pressure on the oesophagus. Pain along an intercostal nerve is rather frequent; it increases in severity if malignant changes supervene. Occasionally Horner's syndrome (from involvement of the inferior cervical ganglion) or pain from brachial plexus involvement has been noted.

*Case V. Fibroma arising from brachial plexus (fig. 7).*—Patient, female, aged 40, had complained for three years and six months of neuritic pain, loss of power in the right arm and hand, and there was evidence of involvement of the oculo-pupillary fibres of the



FIG. 7 (Case V).—Neurofibroma arising from brachial plexus.

sympathetic (miosis in the right eye). There was a palpable tumour above the right clavicle, and extended observation showed that it was growing very slowly. The X-ray photograph showed an upper mediastinal tumour extending upwards into the thoracic inlet. It had a slightly wavy contour, and did not move when the patient swallowed, but displaced the trachea and oesophagus slightly to the left. In the oblique view, there was anterior bowing of the trachea and oesophagus, of a type which is rarely seen in cases of benign mediastinal tumours, but is reminiscent of that seen when there is a right-sided aorta. The tumour was removed and found to be a fibroma. No nerve-fibres were actually discovered in it, but I include it among the neurofibromas because it was attached to and apparently growing from the brachial plexus at operation.

The sympathetic changes, Horner's syndrome, and the brachial plexus changes have come to be associated in the minds of radiologists with what Pancoast has called "the superior sulcus tumour"—a carcinoma of the lung apex, but it occurs in many

other conditions and has often been noted in cases of mediastinal neurofibroma and secondary malignant disease of the upper mediastinal glands invading the posterior mediastinum.

A special case of the neurogenic mediastinal tumours is the so-called hour-glass or dumb-bell neurinoma. This arises from the sheaths of the spinal nerves close to their point of emergence through the intervertebral foramen. The lesion is nearly always single and it tends to grow in two directions : (a) into the neural canal, and (b) towards the chest and under the mediastinal pleura. The effects are summed up in the diagram (fig. 8). The projecting growth in the spinal canal produced symptoms of pressure on the cord, and the few cases I have seen personally came to me from Mr. Geoffrey Jefferson's neurosurgical clinic, the symptoms of onset having been neurological.

The constricted portion of the tumour, the "waist" of the hour-glass, lies in the intervertebral foramen, which it erodes and enlarges. The external portion may

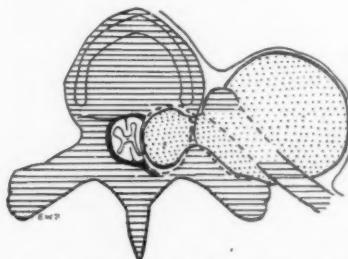


FIG. 8.—Erosion of vertebra and rib by "hour-glass" neurofibroma.

erode the ribs and the transverse processes and often causes widening of the corresponding rib-space—a very typical and characteristic finding. The external portion of the tumour may be quite small, but can usually be found if careful search is made in oblique views.

*Case VI* (fig. 9, a, b, c) illustrates these bone changes. The patient was a woman, aged 59, who had noticed multiple subcutaneous nodules for two years. These were painless, but were increasing in size and number. The skin was pigmented. One nodule was excised and found to be a fibroma. A diagnosis of von Recklinghausen's disease was made. Routine X-ray examination showed the presence of a posterior mediastinal tumour. In the antero-posterior film the tumour is seen projecting on the right side, the pedicles were eroded and the 6th rib space was widened. In the lateral view there was hollowing of the bodies of the dorsal vertebrae with partial forward dislocation of the upper vertebrae on to the lower, owing to the gross destruction of the articular processes.

There was apparently no intraspinal tumour in this case and there were no signs of compression of the cord. The association of a spinal tumour with multiple neurofibromatoma is interesting.

A similar case has been published by Kienböck and Mayer :

It was in a young man who had had pain in the back, weakness, and wasting, for some years. X-ray examination showed large nodular tumour masses in the posterior mediastinum, retropleural and extending in front of and alongside the vertebrae through the entire dorsal region. There was scoliosis and there were multiple erosions of the lateral aspects of the vertebral bodies, heads of the rings, and many articular processes. The diagnosis lay between lymphogranulomatosis and multiple neurofibromatosis. There were no changes in the skin or subcutaneous tissue, and no nodules were palpable. There was no pigmentation.

Another similar case was published by Gorlitzer. In that case also there was subcutaneous neurofibromatosis.

Neuroblastoma (neurocytoma) arising from the sympathetic chain is found most commonly in infants and young children. It may originate in any part of the sympathetic system, and it is highly malignant. Two cases in children aged 5 years, each presenting a rounded shadow at the apex, due to primary sympathetic neuroblastoma, have been described by Hartung and Rubert. Metastases were present



(a)

FIG. 9 (Case VI).—Neurofibroma of "hour-glass" type.

subperiosteally in the long bones and skull, resembling those found in the Hutchinson type of adrenal tumour. Most cases are not of the "hour-glass" type and produce no bony changes in the spine.

Hart and Ellison<sup>2</sup> have described a case of mediastinal ganglio-neuroblastoma in a boy aged 6.

The tumour lay in the left posterior mediastinum and cast a large shadow—partly obscured by the heart but readily seen in the oblique views—suggesting posterior mediastinal effusion. It was shelled out without difficulty. It was of sympathetic origin and apparently metastasizing to glands. Pains in the left leg were present, suggesting possible extension through the intervertebral foramina, with compression of the cord. There was no obvious involvement of the vertebrae.

*Ganglioneuromata.*—The ganglioneuromata arise from the sympathetic chain and are found extrapleurally on the posterior chest wall, usually in the neighbourhood of the costo-vertebral sulcus. In the anterior view they are generally seen as rounded

<sup>2</sup> *Lancet*, 1937 (i), 1458.



FIG. 9 (Case VII).—(b) Neurofibroma: Erosion of heads of 4th and 5th ribs. (c) Erosion of pedicles and posterior surfaces of bodies of 4th and 5th dorsal vertebrae, with forward displacement.

Lateral view

(b)

(c)

well-defined tumours, but in oblique or tangential views they tend to be semicircular, with a broad base in contact with the chest wall.

This flattened shape is also seen in localized parietal encysted effusions and in primary and metastatic tumours arising from ribs, and a diagnosis may be not at all obvious from a single X-ray examination. This hemispherical shape does not exclude an intrapulmonary condition. A hydatid cyst is not always circular; if one side is in contact with the mediastinum or the interlobar surface of the lung or the chest wall, its shape is modified by the pressure, and one side may be flattened. This is shown in the accompanying illustration from a case of hydatid cyst (fig. 10). The antero-posterior view shows a very clearly defined circular shadow, but in the lateral view the cyst has one side flattened against the chest wall.



FIG. 10.—Hydatid cyst of lung. Lateral view: Flattening of cyst against chest wall; resembles a large neurofibroma. Note second cyst at base.

*Tracheobronchial and oesophageal cysts.*—Ciliated cysts of slow growth arising from the entoderm of the gut in a very early stage of foetal development may persist and grow in adult life, and be found attached either to the air tubes or to the oesophagus. I am informed by Mr. J. E. H. Roberts that in very early foetal life the gut is ciliated, and that even in adult life patches of ciliated epithelium may be found in the normal oesophagus. These cysts, which are attached to the trachea or bronchi, tracheobronchial cysts, are probably laid down as aberrant buds from the gut during the formation of the primitive tracheobronchial tree. He has kindly lent me slides illustrating two cases which he himself is publishing in detail.

One was in a young woman who was known to have had an upper mediastinal tumour for some years. In the first film taken this looked very much like a neurofibroma. There were no rib changes. About six weeks afterwards, a second film, showed a sudden diminution in size of the tumour.

Mr. Roberts concluded that nothing but the rupture of a fluid cyst could have accounted for this diminution, as no X-ray therapy had been given. He therefore operated and found,

attached to the trachea, a smooth-walled cyst lined with ciliated epithelium. This he successfully removed.

In the postero-anterior radiogram the oesophageal cyst showed a rather faint shadow projecting on the left side, low down in the mediastinum, with a curved free border seen just below the heart's apex. In the lateral view it overlapped the heart, but cast only a barely discernible shadow. The section showed part of the lining wall of the cyst with its ciliated epithelial lining composed of a few layers cells, with large, rather flattened nuclei. These cysts are very rare. I have never met with a case of this nature before.

*Rare conditions simulating mediastinal tumour.*—In the diagnosis of mediastinal tumour the following rare conditions must be considered : Innominate aneurysm, cardiac aneurysm, neoplasm of the pericardium, pericardial diverticulum, mediastinal effusion, interlobar effusion at the upper end of the main interlobe near the mediastinal surface of the lung, hydatid cyst near the mediastinum, and gumma.



FIG. 11.—Encysted mediastinal effusion.

**Diverticulum of the pericardium** : This is a rare tumour, described by Kienböck and Weiss. It shows a projection from the cardiac shadow, which is rounded, sharply defined, and pulsating. It usually occurs on the right side ; the aorta is not enlarged. It results from chronic adhesive pericarditis. One of the three patients whom these authors first saw in 1929 has recently been re-examined, and the film shows the appearances which they consider typical. A shadow with a convex slightly lobulated contour projects from the right heart border. A fine line of calcification outlining the inner wall of the serous pericardium is bordered by a thicker outer non-calcified shadow of the fibrous layer ; in the lateral view the diverticulum lies in contact with the anterior chest wall.

Morris, in this country, has published a case having rather similar appearances. The first line of calcium was clearly visible in the radiogram. In the lateral view the shadow lay over the origin of the ascending aorta. It seems probable that this case is also a pericardial diverticulum. A pericardial origin was considered possible by Morris. Jansson described a case of pericardial diverticulum in a girl aged 15, and observed that during inspiration the shadow became long and narrow, but widened again on expiration. This "moulding" with inspiration proved the swelling to be of a soft or fluid consistency, and was a point in the differential diagnosis against tumour. The diverticulum consisted of two pockets, one of which, having a freer communication with the pericardial sac, pulsated more freely than the other. There was no trace of calcification in the wall.

*Other conditions which might be mistaken for benign mediastinal tumour.*—A chronic mediastinal effusion or mediastinal empyema may project, with a well-defined semi-circular outline. It may lie in either the anterior or posterior mediastinum or in both. I have slides illustrating two cases, in each of which the history and clinical picture, and the blood-count, taken in conjunction with the X-ray findings, left little doubt as to the diagnosis. One case cleared up spontaneously by rupture into a bronchus and the other was successfully drained (fig. 11).

[Figs. 3 (a and b), 4 (a and b), 5, 6 (a and b), 7, 8, 9 (a, b, and c), 10, 11, are reproduced by courtesy of Messrs. H. K. Lewis, from "A Textbook of X-ray Diagnosis", by British Authors.]

#### REFERENCES

- 1 ASSMANN, H., "Klin. Rontgdiagnostik d. Inn. Erkrankungen", 5th Ed., 1934.
- 2 DECKER, H. R., "Primary malignant tumours of thymus gland, with report of two cases", *J. Thoracic Surg.*, 1935, **4**, 445-459.
- 3 EDWARDS, A. TUDOR, "Intrathoracic new growths", *Brit. J. Surg.*, 1927, **14**, 607.
- 4 FLEISCHNER, F., "Interlob. pleuritis", *Ergebn. d. med. Strahlenforsch.*, 1926, **2**, 224.
- 5 FULLER, C. B., and JAGGER, F. F. C., "Case of dermoid cyst", *Brit. J. Radiol.*, 1927, **32**, 176.
- 6 GORLITZER, V., "Neurofibromatosis", *Arch. f. Dermat. u. Syph.*, 1930, **159**, 510.
- 7 HAMMARSKJOLD, B., "Teratomata and dermoids", *Acta Radiol.*, 1924, **15**, 210-224.
- 8 HARRINGTON, S. W., "Surgical treatment of 11 cases of mediastinal teratomata", *J. Thoracic Surg.*, 1934, **3**, 590-611.
- 9 HARTUNG, A., and RUBERT, S. R., "Sympathetic neuroblastoma", *Radiology*, 1935, **24**, 607.
- 10 HEDBLOM, C. A., "Intrathoracic dermoid cysts and teratomata", *J. Thoracic Surg.*, 1933, **3**, 22.
- 11 ILES, A. G. J., "Case of thoracic fibroma", *Brit. J. Radiol.*, 1932, **5**, 460.
- 12 JACOBAEUS, H. C., and KEY, E., "Intrathoracic tumours", *Acta chir. Scandinav.*, 1921, **53**, 573-619.
- 13 JANSSON, G., "Pericardial diverticulum", *Acta radiol.*, 1931, **12**, 50-57.
- 14 KIENBÖCK, R., and MAYER, S. A., *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1935, **51**, 387.
- 15 KIENBÖCK, R., and WEISS, K., "Pericardial diverticulum", *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1934, **50**, 442.
- 16 LENK, R., "Intrathorakal Tumoren", Julius Springer, Vienna, 1929.
- 17 MORRIS, H., "Unusual thoracic lesion", *Brit. J. Radiol.*, 1933, **6**, 479.
- 18 PANCOAST, H. K., "Superior sulcus tumour", *J.A.M.A.*, 1932, **98**, 988.
- 19 PHEMISTER, D. B., AND OTHERS, "Dermoid cyst", *Am. J. Roentgenol.*, 1936, **36**, 14.

Mr. Tudor Edwards said that the great advance of thoracic surgery in late years was due not only to improvements in surgical technique but also to increasing precision in radiological diagnosis. He thought that in doubtful cases radiologists should not delay surgical intervention by asking for control studies after appreciable intervals.

In his opinion, lipiodol was used rather too freely for bronchographic investigation in certain clinics.

Dr. S. Vere Pearson said that he could corroborate what Mr. Tudor Edwards had said regarding the use of lipiodol being sometimes too free. So far, at all events, as pulmonary tuberculosis was concerned, it was usually, he considered, unwise to

give an injection of lipiodol. Though there might be exceptional circumstances demanding it, they were, he considered, rare.

Regarding the phrenic operation: They had been shown photographs of a wonderfully good result in the case of a large apical cavity. Now the fashion to-day was to be chary about performing a phrenic operation—even a phrenic crush—unless one was quite certain that at no future stage in the patient's history any apical thoracoplasty or similar operation would be found necessary. In the discussion reference had been made to the kymograph. He wondered how far it would be possible by means of this apparatus to obtain information helpful in the classification of cases likely to benefit or otherwise by a phrenic operation.

## Section of the History of Medicine

President—A. P. CAWADIAS, O.B.E., M.D.

[November 8, 1937]

### A Hebrew Antidotary. Queens' College, Or. 5

By HERBERT LOEWE, M.A.

THIS MS. was discovered in the binding of a collection of Hebrew philosophical pamphlets<sup>1</sup> in Queens' College Library. Following the invention of printing, many MSS. were destroyed and used to form the bindings of books, but they can often be detected and recovered. The present writer has rescued two leaves of a twelfth century Missal from the binding of Hutter's Hamburg Hebrew Bible and 40 leaves of an incunable Hebrew Bible of which only three copies are known.

The MS. in question (Queens' College, Or. 5), forms a fragment of what must once have been a fine medical encyclopædia. Unfortunately the surviving leaf is not an example of what the medical skill of the writer was at its best, since it deals with the theriac and the mithradate. It is interesting to note that the theriac was expunged from the London pharmacopeia in 1746, mainly as the result of its exposure by William Heberden, who was trained in the school of Vigani. Vigani was the first Professor of Chemistry in Cambridge (1703–12). He was "An adversary of the alchemists and took experiment as his guide". Vigani's chest of *materia medica* is still preserved at Queens' College and it is ironical to note that this MS., dealing with the theriac, was recovered within a stone's throw of Vigani's chest. In his denunciations of the theriac this, one of the oldest formulas for it in Cambridge, stood at his elbow.

The MS. is written in the Hebrew characters, Rabbinic script, Spanish North-African hand of the early thirteenth century. The writer must have been a Jewish doctor who studied in the Spanish medical school. This may be inferred from some of his technical terms, taken from the Romance Languages. One of these, Lavender, is called Esticados, a Spanish term. Another, *Peganum harmala*, rue, is rendered Ruda; this word also is Spanish, the Italian form being Ruta.

The antiquity of the MS. may be inferred from the following circumstances. In line 16 of the verso, the theriac of Ezra is given. Now in the British Museum MS. Or. 46 (Margoliouth No. 1021, p. 349), which contains the antidotary of Nicholas of Montpellier in the Hebrew translation of Jacob the Less, the same formula is given, but in the title it is ascribed to the "Late Ezra the Prophet". The curious title Prophet or Profacius, Prophète, Profiat, Han-Nabi, is not yet satisfactorily explained. It was borne by quite a number of men, the best known being Jacob b. Makhir. There was a certain Ezra the Prophet of Moncontour who is not, however, known to have been a doctor. He is cited by Meir of Rothenburg (1215–1293) as "my master". He was a tosafist or glossator to Rashi's Commentary on the Talmud.

It is not certain that this Ezra was the author of the theriac known as Ezra's theriac, but it is very unlikely that the relatively rare name Prophet should have been applied to two people called Ezra.

Presuming the identification to have been established, then this MS. must have been written during Ezra's lifetime, since the usual formula "his memory for a

<sup>1</sup> The shelf-mark is Or. 6. iii, 12: the pamphlets are (1) *Sefer Ma'yan ha-Hokhmah*, Amst. 1651: *Sefer ha-Bahir*, Amst. 1601: *Sefer ha-'emunoth, Sa'adya*, Const., 1562.

blessing" is not used, as it is in the British Museum MS. If this is correct, the MS. belongs to the early part of the thirteenth century.

The medical terms used in the MS. are drawn from a variety of languages, Hebrew, Syriac, Arabic, Turkish, Persian, Indian, and Romance; the interpretation has consequently proved a matter of considerable difficulty. Certain examples were adduced.

(a) Armoniaq, which might be:—

- (1) *Ferula tingitana*.
- (2) *Dorema ammoniacum*.
- (3) *Prunus Armeniaca*, i.e. apricot.

(b) Ga'dah: this might be:—

- (1) *Teucrium polium*.
- (2) Chamaedrys.
- (3) Germander.
- (4) Veronica or Speedwell.

(c) Kafar al Yahudi: this might be:—

- (1) (with K), Camphor, because Jews traded with it in Marseilles in the thirteenth century.
- (2) (with Q), Bitumen of Judaea, Jews' pitch asphalt.

There are many MSS., those already mentioned and others, e.g. University Library, Cambridge, Add. 1221, Bibliothèque Nationale Hebr. 1134, &c., with which this antidote may usefully be compared. As regards Maimonides, it may be remarked that his prescription does not contain the ingredient of Viper's Flesh or venom, although in his Commentary on the Mishnah, Maimonides goes out of his way to emphasize the medical value of snake products.

The following is a specimen of the Antidote:—

QUEENS' COLLEGE Ms. Or. 5

1 Mithkal  $\frac{1}{2}$  = 78 grains      1 Zuz or dâniq = 10 grains

RECTO

Lines

- (15) MITHRIDITUS (antidote). This is the troche invented by (lit., the work of) the honoured Mithradates and (which was) called after
- (16) his name. And they compounded [sc. it. Or, 'and he compounded it'] of drugs which had been tested against poisons
- (17) of divers kinds and against various diseases. And this became the theriac at that time. Later, in the preparation of
- (18) Andromachos, in view of his realization of the virtue of viper's-flesh and other ingredients, there was (sic) added to it (i.e., to the antidote), troches of
- (19) viper. He (Andromachos) made slight changes, by increasing or decreasing [the quantities]. But the "Great Theriac" was more efficacious than it (i.e., than the original formula of Mithridates)
- (20) in one respect, and that was [in its containing] snake's venom (not merely snake's flesh). Now in regard to the other ingredients, the antidote should not lack
- (21) —nor should the Theriac—any appreciable amount (i.e., the quantities should not be diminished to any considerable extent): it may, rather, be augmented. In many of the ingredients there is efficacy and [their increase] is more productive of benefit.
- (22) [It would take too] long to [re-] enumerate for the theriac those ingredients which have already been mentioned (i.e., for the antidote) but [the quantity of each] may be slightly augmented.

- (23) THE ANTIDOTE-TROCHE, common formula. Let there be taken:— myrrh and *polyporus officinalis* (agaric), and *zingiber officinale* (ginger) and cinnamon
- (24) and *amygdalis Persica* (peach), in equal weights, 10 *zuzim*, spikenard and *Boswellia Carteri* (frankincense), *portulaca oleracea* (purslain)
- (25) [clusters ? of] *Schenanth*, balsam-wood and *lavandula stoechas* (lavender), and *tordylium officinale* (seseli) and *sassurea lappa* (costus) and *Ajuga*, (chamaepitum) and *galbaniflua ferula* (galbanum)
- (26) long pepper and extract of *tragopogon* (goat's beard) and *castoreum*, Indian spikenard and *styrax officinale* (styrax), and *opopanax*, in equal weights, 8 *zuzim*.
- (27) [*Cassia lignea*, pepper, white and black and *colchicum* sp. (hermodactyl) and *teucrium* sp. (germander), and *allium* sp. (scorodon or garlic ?), and *daucus* and *trigonella* sp. (melilotus, sweet clover or rosemary ?).

[March 2, 1938]

## TWO ENAMEL MINIATURES OF MEDICAL MEN

- (1) Sir Theodore Turquet de Mayerne (by Petitot)  
and
- (2) Dr. Richard Mead (by Zincke)  
by

SIR STCLAIR THOMSON, M.D.

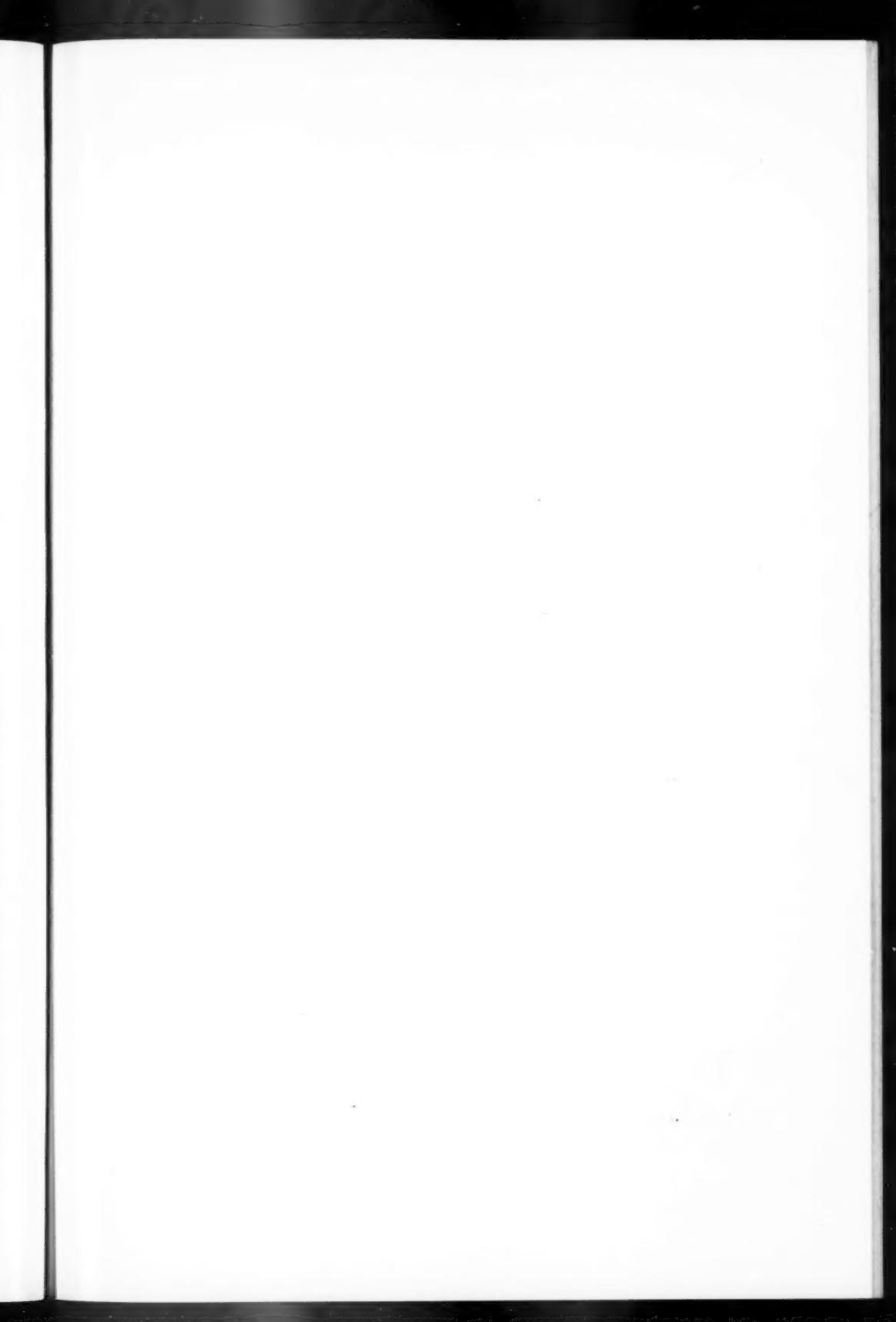
MINIATURES in enamel are not as common as those painted on cardboard or on ivory. This is doubtless due to the difficulty of their production, to which I will refer presently. They are also much rarer than prints or engravings. These latter, one might say, are abundant, although of different degrees of excellence. They are particularly interesting to the medical profession as we find amongst them a large number of portraits of leading men of our calling, dating from the days of the Renaissance until the engraver's art was killed by the development of the mechanical craft of photography. The library of the Royal Society of Medicine contains a collection of about 4,000 prints of medical celebrities, in line and mezzo-tint, beautifully arranged and well catalogued. There is a fine collection of more than 5,000 engraved portraits of medical men in the Royal College of Physicians. The late Lord Moynihan was a well-known collector and so was Sir John Thomson-Walker who made the choice collection which he has bequeathed to the University of Edinburgh. Dr. Arnold Chaplin was the happy possessor of many beautiful specimens which he has generously given to the Royal College of Physicians and the Medical Society of London.

Miniature portraits of doctors are rarely met with in museums or auction rooms, especially when compared with the number of those of pretty ladies or of royal, noble, or popular personalities. This is my excuse for bringing before you the two I have lately secured.

Miniature painting, i.e. portraits made in water colour or in oil, on ivory, or more rarely on cardboard, is a subject of much interest but does not come under our consideration this afternoon. Miniature portraits in enamel have, over them, the advantage of being permanent and of not losing their brilliance or fading, as the usual miniature is inclined to do, if exposed to light. Portraits in enamel are made on a metallic basis—copper, silver, or gold. On this a vitreous base of white is spread and fixed by firing. On this foundation the portrait is made by an infinite number of delicate touches with a fine brush, applying the necessary metallic salts—oxides as a rule—mixed with a flux to hold the grains together and make them adhere. Then,

by heating the preparation in a kiln or oven of a correct temperature, the colours are fused and fixed. This fusing is a delicate matter, partly because the different colouring materials employed fuse at different temperatures, and partly because the resultant colour may change with the temperature employed. Hence, the colour finally obtained and the fixation depend a good deal on the technique of the correct firing. This firing may have to be repeated seven or eight times. The colours employed are prepared by mixing the finest sand with soda or potash and grinding it to a fine powder with the requisite oxide of cobalt or arsenic or copper, &c. Now, the colour of this prepared pigment may change, under the influence of heat, from what it was when picked up on the brush. Besides, when these oxides are ground into a fine powder their colour is no longer easy to recognize and, if each different saucer of colour is not carefully labelled and watched, the artist may make a mistake and find afterwards that he has picked up on his brush what turns out to be a blue pigment for the face and a pink one for the hair! Again, fusion may be either incomplete or may be overdone so that the colours run. Finally, the heat may be miscalculated, spoiling the picture or damaging its metallic basis and so ruining the whole result. This is particularly difficult to avoid, as the field of work is so small and requires such minute touches. In addition, the art of the portrait painter requires such constant care, close attention, and technical skill to make a complete picture that several failures may be encountered before one successful enamel portrait is produced. There were probably large numbers of failures of which, naturally, there is no record. Finally, a clear vitreous flux is poured over the completed picture and fixed on by firing, to make a protective glaze.

The first enamel I show is that of Sir Theodore Turquet de Mayerne (1573-1655), whose history and personality are so well known that I need only briefly refer to his biography. Born near Geneva on September 28, 1573, he was the son of a Protestant historian, of Italian origin, who had escaped from Lyons to Geneva at the time of the Massacre of St. Bartholomew. After studying at Heidelberg for four years he obtained his M.D. at Montpellier in 1597 (aged 24). His teacher, Rivirius, removed to Paris where he was attached to the court of Henry IV. This connexion probably explains why Mayerne, who followed his teacher to the capital, within a few years obtained an appointment as a junior Royal Physician (1600). He began to teach pharmacy and to defend the use of chemical remedies, especially mercury and antimony, which were at that time abhorred by the Galenists. Irritated by an anonymous attack in 1603 (he was then 30) he published a defence in a treatise of 120 pages. This began with a reference to the jealousy which, as a graduate of Montpellier, he had been received by the Faculty of Paris and then he went on to show that the use of chemical remedies was not only in accord with the principles but also with the practice of Hippocrates and Galen. This brought down upon him a reply, "Ad famosam Turqueti Apologiam responsio", filled with abuse, beginning with a bad pun on his name (turquet = a cur), pointing to errors and bad grammar in his writing and charging him with having damaged several patients with his treatment. Promptly the College of Physicians, in the University of Paris, condemned this "apologia" of his by a unanimous vote, ordered physicians to refuse to meet him in consultation, and recommended that he should be deprived of his office of "Royal District Physician". He must have felt this enmity; he ceased to lecture and took no further notice of the attack. Doubtless he was therefore glad when, in 1606, an English peer whom he had cured in Paris suggested his removing to London. The assassination of his patron, Henry IV, and the necessity of becoming a Roman Catholic if he succeeded to the post of Chief Court Physician, doubtless led to his welcoming this opportunity for leaving France. His noble patron in England presented him to the King and in the summer of 1611 he was appointed first Physician to James I. He had already been incorporated M.D. at Oxford on April 8, 1606, and that he should be elected an F.R.C.P. in 1618 shows how our profession has always





Sir Turquet de Mayerne (1573-1655).  
(Slightly enlarged.)



Dr. Richard Mead (1673-1754.)

*Sir StCLAIR THOMSON: Two Enamel Miniatures*



been free from much of our insular prejudice against foreigners. It appears that he soon secured a large and select practice. It is recorded that his income was "at least" £5,000 a year and that when his daughter married she was regarded as an heiress. He was knighted in 1624. He was later appointed physician to Charles I and his command of French must have helped to gain the esteem and friendship of Queen Henrietta Maria. He continued his chemical researches; brought calomel into use and was the first to prepare "black-wash" by mixing lime-water with mercury. In view of this present exhibit it is particularly interesting to read that he made experiments relating to pigments and enamels. He discovered the colour principle necessary for the carnation tint in enamel painting and, between 1620 and 1646, he wrote a large manuscript volume entitled "Pictoria Sculptoria" which contains records of many trials of pigments. He was a copious note-taker and 23 volumes of his notes can be studied in the British Museum. He always wrote in Latin or French, and the evident fact that he never became perfectly familiar with English shows that this did not prevent him having a full professional life, active in practice and in public duties and in the study of medicine and allied sciences.

Norman Moore says "Mayerne was a great physician and the general tone of his writings is enlightened. He was an innovator and a man of new ideas" (*Dictionary of National Biography*). He was not above prescribing cosmetics for the Queen. He gained and retained the good opinion of contemporary physicians. A good portrait of him hangs on the staircase of the Royal College of Physicians and a fine drawing, by his friend and contemporary, Rubens, can be seen in the British Museum.

It has been suggested that Mayerne has been portrayed by Shakespeare as "Dr. Caius" in the *Merry Wives of Windsor*. If so, it must have been as a caricature, for his whole record is very different from what one would expect from such a figure of fun as the physician in Shakespeare's play. Amongst other evidence of his good standing in the profession I might refer to an incident in his career which I described in a paper on "Antimonyall Cupps" read before this Section in 1926.<sup>1</sup> This shows how he brought before the College of Physicians the behaviour of such quacks as "the sellers of purging Diet-Ales and such Comfit-makers as sold purging confectioms", and how this met with the support of the President and Fellows and, through them, to action by the Archbishop of Canterbury.

Mayerne's skill and knowledge in pharmacy explains why he was consulted in the composition of the sacred oil employed for anointing our kings at their coronation. In early times this was composed of balm of Gilead and olive oil, was known as "the Holy Oil out of the Sanctuary" and was employed at the rite of coronation of monarchs from the time of Edward the Confessor until after the Reformation. It was not until the seventeenth century that a change took place and it was decreed that a new oil be consecrated for the coronation of Charles I. Sir Turquet—who had then been lately associated with Gideon de Laune in founding the Society of Apothecaries—was consulted and originated a prescription for the anointing oil which has never been superseded. It is composed of orange and jasmine flowers infused in oil of ben (sesame seeds), the distilled oils of rose and cinnamon, prepared benzoin, ambergris, civet, musk, and spirit of rosemary. This forms a most fragrant compound and will keep almost indefinitely. It was used for the anointing of Charles I and Charles II. James II had to obtain absolution from Rome, as this oil had been consecrated by a non-Catholic bishop. This same oil was employed at the Coronation of William and Mary, Queen Anne, George I, George II and George III and George IV. There is no record of the composition of the oil used at the coronation of Queen Victoria, but it may be presumed that it was prepared from the same formula. The oil used for anointing at the coronation of King Edward VII was made up by Squire and Sons, the King's chemists in Oxford Street. It was prepared from Mayerne's formula

<sup>1</sup> *Proc. Roy. Soc. Med.*, 10 (Sect. Hist. Med.), 123-128.

with but a slight addition. Some of the same oil was again employed at the coronation of George V, and last year at the crowning of George VI. It has a rich perfume of peculiar fragrance and is of an amber colour.

The ampulla from which the oil is poured into the anointing spoon holds a little over three ounces. From early times it has been customary always to leave in it some of the original composition and to add new oil as required. In this way the sanctity of the oil is maintained.<sup>1</sup>

Turquet remained in London through the Great Rebellion. After the execution of Charles I he was appointed physician to Charles II. His London house was in St. Martin's Lane but, on his retirement, he settled in the village of Chelsea and died there on March 22, 1655, aged 82. He bequeathed his history to the Library of the R. College of Physicians and unfortunately it was destroyed in the Great Fire. He is buried, with his wife, his mother, and five children, in the Church of St. Martin's in the Fields, where there is a monument on the north wall of the chancel with a long, Latin inscription.

This remarkably small portrait of Mayerne—it is an oval and less than an inch in length—is doubly interesting because it was made by a fellow townsman and co-religionist of his. The great enameller Petitot was of French origin and was born in 1607 or 1609 in Geneva, where his parents, having adopted the Protestant faith, had taken refuge. He came to England in 1635 and received invaluable help from Sir Turquet who introduced him to Charles I. This King, whose taste in art is well known, appreciated Petitot's ability so much that he gave him an apartment in Whitehall. Mayerne also introduced Petitot to Van Dyck, of whose celebrated portraits he reproduced many enamels. The two friends worked together on the nature and properties of metallic oxides with such success that the miniature-painter's palette became greatly enriched so that he was able to express all the shades of flesh-colouring in a way which, as one writer on art says, "had never before been approached and has never been excelled" particularly when one regards the exquisite finish and minute effects produced with so difficult an art as that of fusing colours. The expression of life and character obtained in this minute work is more striking if one compares it with the insipidity, sameness, and monotony, of the large oil portraits of his contemporaries, Sir Peter Lely and Sir Godfrey Kneller.

Owing to the troubles of our Civil War, and to the loss of patronage of Charles I, Petitot returned to France in 1645 and was well received by Mazarin and Louis XIV, who gave him an apartment in the Louvre. Commissions poured in and this was the most productive period in his career. In 1685, on the revocation of the Edict of Nantes, he would have left France on account of his Protestant faith, but le grand monarque was unwilling to part with him; he shut him up, for safety, in Fort l'Evêque and sent the eloquent Bishop Bossuet to convert him! Worn down by imprisonment, and to regain his liberty, Petitot recanted and having "signed like the rest" he was allowed to escape to Geneva in 1687, after forty-two years' work in Paris. In Geneva he was received back into the Huguenot communion and was soon overwhelmed with commissions although he was in his eightieth year. This vitality was doubtless largely due to his happy nature, for we are told that this octogenarian "soon recovered his high spirits". To avoid being overwhelmed with work he retired to Vevey where he lived four years longer. While engaged in making an enamel portrait of his devoted wife he was stricken with apoplexy and died, in a few hours, in his 84th year. Happy man!

The story of Dr. Richard Mead (1673-1754) need not detain us so long. His life story, falling in the placid days of Queen Anne and the early Georges, is not so

<sup>1</sup> For these interesting details I am indebted to Mr. C. J. S. Thompson, Hon. Curator of the Historical Collection in the Royal College of Surgeons.

picturesque as the happenings and tragedies of the days of the Renaissance. But he was a physician with an interesting career and a character which was admirable and enviable.

Born in Stepney, in 1673, he was the eleventh child in a family of thirteen. His father had been ejected for non-conformity in 1662 but was possessed of large means and so was able to continue to reside in the parish. Here his son was educated at home and in a private school. His classical education must have been better than the average nowadays, as he acquired and retained through his life a love of learning and he knew his Latin so well that he was able to attend lectures in that tongue in Utrecht, Leyden, and Padua, where he graduated M.D. on August 16, 1695. Returning to London the following year he began practice in Stepney. In 1703 he was elected Physician to St. Thomas's and moved to Crutched Friars and, later, to Austin Friars. He was already an F.R.S. In 1707 he was made M.D. at Oxford and, having passed the M.R.C.P. in 1708, he was elected a Fellow in 1716 and served as a Censor. His practice becoming large he moved to the house in Bloomsbury Square formerly occupied by Radcliffe, whom he followed as the owner of the "Gold Headed Cane" which now reposes in the Royal College of Physicians, after having subsequently passed through the hands of Askew, Pitcairn, and Baillie. In 1720 he removed to Great Ormond Street, where his house occupied the site of the present Children's Hospital.

He was a great collector and, though many physicians have been collectors, no one has ever rivalled Mead. His library of 10,000 volumes was sold after his death for £5,518, while his pictures, coins, and antiquities, realized £10,000. He was a great reader, he kept up his classical attainments, he was a social success and he had an enormous circle of devoted friends. He attended Queen Anne, and Pope, who was his patient, refers to him in the line : "I'll do what Mead and Cheselden advise" and also refers to his bibliographical taste when he writes :—

" Rare monkish manuscripts for Hearne alone  
And books for Mead and butterflies for Sloane."

He was acknowledged "as a man to whom all people that pretend to letters ought to pay their tribute, on account of his great eminence in them and patronage of them". He was much sought after for his influence, as he was the one person who could approach everyone.

He saw patients at Rawthmell's Coffee House in Henrietta Street, Covent Garden. His country journeys he made in a coach and four, although he used to drive six horses when he visited his country place at Windsor. He attended George I, George II, Robert Walpole, Sir Isaac Newton, Bishop Burnett, and most of the celebrities of his time. His income was between £5,000 and £6,000 a year. He did not write much, but he was abreast of progress in such subjects as general hygiene and inoculation for smallpox.

He died at his house in Great Ormond Street on February 16, 1754, after an illness of only five days. His age was 81.

The world in which he lived and shone was that of learning, for which his taste began in boyhood and continued to old age. He was a generous man and of the men who have grown rich in the legal, and to a much less extent in the medical, profession, few have expended their riches during their lifetime so generously and wisely as Mead. His hospitality was unbounded. He is reported to have said that he would sooner live rich than die rich, and he appears to have passed his days in the magnificence befitting a wealthy man. It was said of him that he gained more, spent more, and enjoyed more than any man of his day and Dr. Samuel Johnson said that : "Dr. Mead lived more in the broad sunshine of life than almost any man".

This enamel miniature of Mead confirms the short pen-picture I have sketched. It was made by C. F. Zincke, a native of Dresden who came to England in 1706 and

later secured the patronage of George II. He was a prolific worker and had a large clientèle in the days of Queen Anne. During his forty years of practice he must have executed a great number of portraits, for he was the fashionable enameller of his day, so much so that even the raising of his fee could not check his popularity. His eyesight failing him, he retired in 1746, to live some twenty years longer.

His work is characterized by the brilliant blues he was so fond of introducing and also by the striking pinks. His art has been said to have a "spick-and-span style" and in his portraits he tends to repeat the insipidity and monotonous consistency of Kneller. His work cannot compare with that of Petitot.

The art of making enamel portraits started in the days of Elizabeth, reached its height in the reign of Queen Anne, and died out in the mid-Victorian era. Formerly, it carried a Court appointment. The last to hold this was William Essex. He was born in 1784 and in 1839 he was appointed to the office of "Enameller to H.M. Queen Victoria and the Prince Consort". He died in Brighton in 1869, and with him the art of enamelling may be said to have expired in this country. It had never been extensively practised here.

#### BIBLIOGRAPHY.

WILLIAMSON, GEORGE C., "The Miniature Collector", London : Herbert Jenkins, 1921.  
WILLIAMSON, GEORGE, and BUCKMAN, PERCY, "The Art of the Miniature Painter", London : Chapman and Hall, 1926.  
FOSTER, J. J., "Chats on Old Miniatures", London : Fisher Unwin, 1908.  
MACMICHAEL, WILLIAM, "The Gold-headed Cane", New York : Paul B. Hoeber, 1915.

## Section of Laryngology

President—C. A. SCOTT RIDOUT, M.S.

[February 4, 1938]

### The Use of Radium in Allergic Rhinitis with Polypi

By W. G. SCOTT-BROWN, F.R.C.S.

THE treatment of recurrent nasal polypi with radium has been recognized for many years. In 1922 Lyons reported on the result of such treatment over a period of three years at the Mayo Clinic. At that time no distinction was made in the aetiology of recurrent polypi, but two out of three cases suffered from asthma. In a further review ten years later he noted the frequency with which eosinophil cells are observed in sections of mucosa, and also stated that success depends upon the presence and extent of suppuration in the sinuses.

In 1932 Bernheimer reported a series of 44 cases of allergic nasal disease treated with radium, and claimed uniformly good results as to sneezing, rhinorrhœa, and recurrence of polypi. Berven also demonstrated a series of cases at this time which showed that recurrence was prevented.

In the series now reported those cases which responded best gave a typical allergic history and had little or no infection. The cases with severe sinus infection did not give such good results, and in a few the infection was aggravated even though the polypi did not recur. The cases should be divided therefore into those which are apparently allergic in origin and those which are infective, when selected for treatment.

*History.*—A family history of asthma, hay fever, spasmodic rhinorrhœa, or even recurrent nasal polypi is found in a number of these recurrent cases. There is frequently a past history of allergic manifestations, such as asthma, infantile eczema, urticaria.

*Symptoms and signs.*—Nasal obstruction is often associated with sneezing attacks and rhinorrhœa. As in all allergic manifestations, the periodicity of the attacks is characteristic, and in these cases the rhinorrhœa is frequently on rising.

Clinically the mucous membrane of the turbinates and septum shows the characteristic pallor of allergic conditions. It is seen most frequently in asthmatics or in cases of sneezing and rhinorrhœa and recurrence of nasal polypi. Infection may so easily supervene in the sinuses from the obstruction of allergic polypi that it is often difficult to be certain whether the infection follows or precedes the polypi.

*Pathology.*—Pathological examination may or may not confirm the clinical opinion. The skin tests are of no value if negative, or if indefinitely positive. Occasionally the skin tests give an undoubted reaction of value both in diagnosis and supplementary treatment.

An increase in the eosinophil cells of the blood is sometimes present, but not invariably. These cells are also frequently present in the nasal secretion.

In a number of cases from which mucous membrane was sent for section an abnormal number of eosinophil cells was reported, but a negative report does not exclude a possible allergic basis.

*Selection of cases.*—There should be no clinical or radiological evidence of closed infection in cases selected for treatment with radium. In the apparently clean cases the polypi should be removed, but it is not necessary to open the ethmoid. It is true that if the ethmoid is opened the mucous membrane is often thickened and even polypoid, but the radium makes it shrink.

In clean cases radium is inserted three weeks after the polypi have been removed, but in cases in which any of the sinuses have to be drained it may be wise to wait for four to six weeks. The disadvantage of waiting is that in some cases the mucous membrane becomes polypoid again so rapidly.

*Details of radium used and its insertion.*—The needles used are 3.5 cm. long, and consist of a platinum filter 0.5 mm., each containing 10 mgm. of radium element, the active length being 2.5 cm. Eight needles are inserted in each case, four into each ethmoid capsule.

Each needle is fixed in a holder in which it is inserted and the needles are fixed in position by strapping the shanks of the needle-holder to the nose. The needles are left in position for six hours, thus giving with the 4 x 10 mgm. needles in each side a total of 240 mgm.-hours to each side. In children it is necessary to give rather more by leaving the needles in for seven and a half hours.

Before the insertion of radium the patient is given morphia 1 gr. and the nose is prepared by spraying with cocaine and adrenaline, and then painting the middle meatus right back to the anterior sphenoidal wall with cocaine paste. The needles are then inserted into the ethmoid capsule, the first into the posterior ethmoid so that its point rests on the anterior sphenoidal wall, and the others evenly distributed

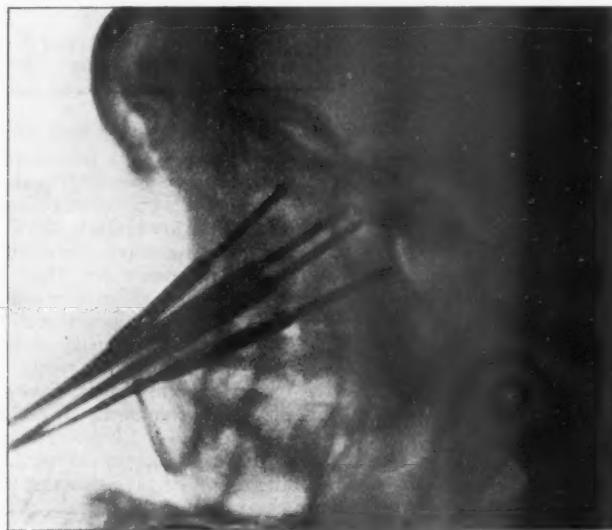


FIG. 1.—Lateral view to show radium needles in their holders in position in the left ethmoid.

so that the anterior needle is just under the anterior end of the middle turbinate. The accompanying radiograms (figs. 1 and 2) indicate the positions in which the needles should be placed.

*Histology.*—This has been investigated in a number of cases by Dr. Joan Ross.

In sections taken from cases, after one or two months, the appearance is that of a simple inflammatory condition. There is a round-celled infiltration in the submucous layer and around the vessels. In addition there are usually small areas of extravasated red blood-cells and the nuclei of the small round cells are degenerated. Both these points are characteristic of a radium reaction rather than a true inflammation.

In sections specially stained for fibrous tissue a fine perivascular fibrosis can usually be made out by the sixth week (fig. 3).

As a result of this radium reaction typical changes are seen after twelve months.

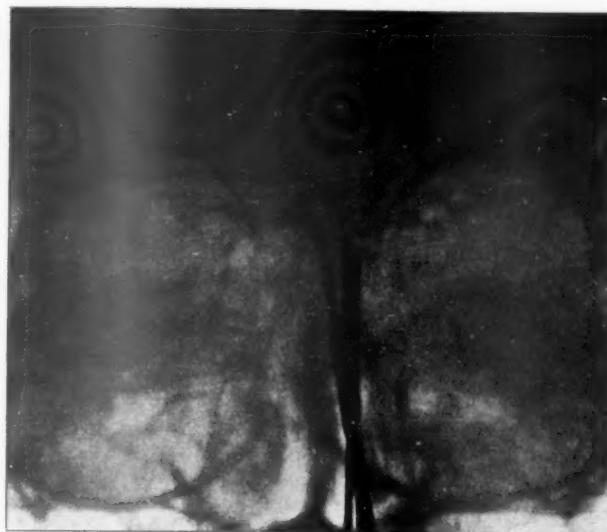


FIG. 2.—Same case as fig. 1, with needles in position in the left ethmoidal tunnel.



FIG. 3.—Section taken from the middle turbinate in a case treated with radium five weeks previously. A, early perivascular fibrosis. B, area of extravasation of red cells. The nuclear degeneration is easily seen throughout the section.

The mucous membrane remains ciliated, while in the submucous layer there is a marked fibrosis. Whorls of fibrous tissue are seen around the vessels and a thrombus is often seen in the large vessels, a characteristic change following radium implantation (fig. 4).

The radium causes swelling of the nasal mucosa and the patients usually have a period of from three to six weeks' discomfort and obstruction, and it is well to warn them that it takes nearly two months before the airway becomes clear.

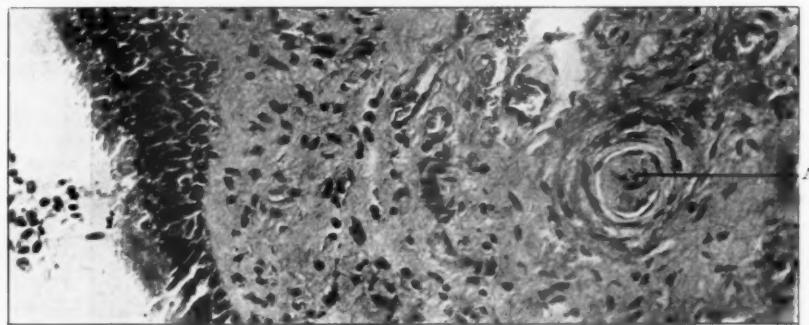


FIG. 4.—A section of mucous membrane from the middle meatus in a case treated with radium fourteen months previously. A, a large vessel containing a thrombus, around which can be seen the dense perivascular fibrosis. The generalized fibrosis, denser in the submucous layer, can easily be made out. The epithelium is ciliated.

*Summary of cases.*—During the past four years 47 cases have been treated. The patients shown to-day are typical of the results obtained in cases without infection or in which the infection was given free intranasal drainage at the time of removal of the polypi.

The earliest cases show that the results are more than temporary. Five of them were irradiated about three and a half years ago, and two of these nearly four years ago. They have had no recurrence of polypi since. Most of them have an allergic basis, but some also had a sinus infection which was dealt with by intranasal drainage at some time in their history. Nearly all the cases shown to-day had polypi removed many times, and several of them say that polypi have been removed dozens or even a hundred times. They were all cases in which the nose was packed with polypi, and in several the polypi recurred in spite of careful removal under general anaesthesia. They are not all entirely symptom-free to-day; some still have allergic manifestations, and in some the infection has not entirely cleared, but none have required further removal of polypi which is the aim of this treatment with radium.

*Discussion.*—MYLES L. FORMBY: As the result of a short discussion with Mr. Scott-Brown about two and a half years ago, 23 cases were treated with radium. The technique employed was determined by the radium available at the time. The procedure was completed at one sitting. If the nose were full of polypi these were removed and the radium implanted immediately. Six 6.5 mgm. needles were placed in each side of the nose, that is, 78 mgm. in all, and left there for seven hours. A piece of dental stent, shaped in much the same way as the ordinary Lake's rubber splint, was used for holding the needles, and pushed into the upper part of the nose, as high as possible. In a wide nose it is possible to place it against the cribriform plate, and keep it in position by packing with paraffin gauze. With one exception—in a child—all the cases treated have been satisfactory. One of the complications which arise is the development of adhesions. This is possibly due to the technique employed. The patient is given a full dose of morphia about three-quarters of an hour before the stent is extracted, but it is difficult in some cases to effect removal, and there is a little bleeding and scratching of the mucous membrane. Possibly the practice of inserting the radium at the same time as removal of the polypi accounts for more reaction than in Mr. Scott-Brown's cases.

In other cases division of the adhesions has been performed subsequently. There has been no hurry to divide them lest some degree of atrophic rhinitis might develop.

ERIC WATSON-WILLIAMS said that he had treated a number of patients by this method a few years ago, but had abandoned the treatment, perhaps prematurely. His first cases were treated in 1932, and although he got some good results, in others the results were

disappointing. He came to the conclusion that his dosage was insufficient, and in 1933 he started with a larger dose, amounting to about four times that which had been described at the present meeting— $1\frac{1}{2}$  to 2 grm.-hrs. He used six needles of 6.25 mgm. with 0.6 mm. filter in a wire frame, three on each side; or if one side only was affected then four on that side. The wire frame was made of a malleable silver wire, and permitted a close fit into the nose, with fixation on the upper lip. This meant an exposure of a day-and-a-half, or sometimes two days. The results were good from the point of view of cure of the polypi. He had lately checked the results, and apart from one patient who had since died, and one who had not replied later than two years from treatment, all were completely free from polypi.

There was another side to the question. Two of his patients, although they were free from symptoms—one for two years, and the other for three years, after treatment—had gone on to a severe nasal atrophy. A case which gave special trouble was in a patient he treated during the latter part of 1934, using a dose of only 1.5 grm.-hrs. A year later the patient, who was perfectly free from all symptoms in the nose, came up complaining of a sore patch in his mouth, and developed a perforation of the hard palate. It was difficult to say why the palate alone was affected unless the perforation was syphilitic, because the X-ray photographs of the case show the radium needles right up in the top of the ethmoid.

This circumstance had made him reserve this treatment for a few special cases unsuitable for ordinary methods, and so he had used it comparatively seldom since the end of 1934. In 1936 a man, then aged about 27, whom he had treated early in 1933, came up complaining of a disagreeable smell in his nose, and proved to have a small sequestrum of the vomer, which was removed. He came up again in September 1937, and this time he had a perforation of the palate, with a further small bony sequestrum. It seems impossible to doubt that the damage was due to the radiation. The event showed the need for caution in using such a potent agent as radium in cases where its use was not absolutely essential. In the first of the cases he had related he was fairly easy in his mind because, apart from the condition described, there was nerve deafness which had been diagnosed as specific, and he felt that he had at most precipitated a necrosis which in any event would have occurred in time. But in the second case there was no history of syphilis, no complement reaction, and no other stigmata. He felt it very necessary therefore that the dosage in such cases must be kept strictly to the minimum that would give the results desired.

RITCHIE RODGER said that he had questioned the patients in seven of the cases shown, as to whether the sense of smell was present, and five had replied in the affirmative. Moreover, the mucous membrane looked healthy. His own junior colleague, Mr. R. R. Simpson, had been working on similar lines and he thought he had about sixty cases up to now, and was very hopeful about the results. He used a cylindrical carrier for 10 mgm. of radium on each side of the nose, and he gave about twenty-four hours' exposure—altogether 240 mgm.-hrs., the same dosage as Mr. Scott-Brown. There was a danger, however, as Mr. Watson-Williams had explained. Cases of active suppuration with polypi should be carefully avoided. By a mischance, one case which was assumed wrongly by the house surgeon and the sister to be a radium case, but which Mr. Simpson had not intended to be treated by radium, was so treated in his absence. Necrosis of the ethmoid region and the cribriform plate developed, and the patient died. It was very important to beware of active suppuration in the sinuses.

A. LOWNDES YATES said that it was important to get some idea of the "r" units which were being used, because screening was a vital matter. This calculation was made by the weight of radium, the time of action, the screen employed, and the distance from the tissues. He thought that even smaller doses than Mr. Scott-Brown had used produced good results. If small doses were not used, however, atrophy occurred after a long time, and if very large doses were used the ciliated epithelium was killed. It was clear that Mr. Scott-Brown's dose was about right. The amount of radiation that the ciliated epithelium would stand was enormous. Twenty erythema doses might be given and the epithelium would still remain active; with above that amount it died. The amount of radium which Mr. Scott-Brown used could not produce that effect.

Secondary rays were given off from any metal on which gamma rays struck, and if there were a large number of these secondary rays from metal screens impinging on the nose some necrosis was likely to follow. What was apparently a very small dose of radium might, when acting close to the tissues, be a very big dose indeed.

**Persistent Suppuration of Right Maxillary Antrum after a Caldwell-Luc Operation.**—C. de W. GIBB.

Female, middle-aged.

Right intranasal antrostomy by another surgeon in 1933. Seen 28.10.36, when she had had pain in the right cheek and right side of the nose, and copious haemorrhagic discharge from the right nostril. There was a large opening into the right antrum; this was syringed out with an antral cannula, and some pus came away. The right middle turbinal was large and cystic.

The pain and discharge continued intermittently, and on 30.12.36 it was arranged to have an X-ray examination of the sinuses.

X-ray report (31.12.36): "There is definite loss of transradiency of the right antrum, but I can see nothing else abnormal. I think the right ethmoids are healthy."

In January 1937 a right Caldwell-Luc operation was performed and the right middle turbinal was removed. After the operation the antrum was washed out at times. Often the lotion returned clear, and the patient would then blow out a large coherent mass of mucopus.

She has since been to see me at various times and has sometimes brought a bottle containing about two drams of pus, which she has stated to have come from her nose a short time previously.

*Discussion.*—The PRESIDENT said that he was looking at this case with Mr. Gibb, and it certainly presented a problem as to whether the pus was coming from any other cavity than the antrum itself.

HERBERT TILLEY suggested that the symptoms mentioned were manifestations of a hidden focus of infection which was not obvious during the operation. The pain and discharge of a large coherent mass of mucopus—often the shape of a limpet-shell—betrayed a septic focus beneath mucoperiosteum which lines the alveolar groove and is nearly always to be found in the molar region.

In this situation he had sometimes detected a single abscess, or small pin-head collection of pus which covered an area of carious bone. When portions of this were stained and examined microscopically they were found to be infiltrated by microcoecal organisms (*vide* the "Semom Lecture," *Journ. Laryng. and Otol.*, 1935, 50, 1). This type of local infection would amply explain why in the present case the pain continued intermittently, though the first operation had provided a large opening in the right antrum. He recommended a third operation to seek and remove an infected area of alveolus which seemed the most likely pathological factor.

J. F. O'MALLEY said that he had come to the same conclusion as Mr. Tilley, and suggested that a skiagram of the alveolus should be taken. Sometimes a focus of this type in the alveolus could be distinguished; and there were cases in which there was recurrent evidence of antral suppuration due to the bone underneath. If the infection of the antrum was of dental origin there might be still a focus present. The method of operation mentioned by Mr. Tilley was one which appealed to him. He had made a careful examination in this particular case, with the catheter inside the antrum, and when the catheter had arrived at the junction of the anterior wall and the floor the patient had exclaimed, "That is the point". That was where tenderness was felt. Mr. Gibb had said that he had washed out the antrum and found nothing, and immediately after the washing this secretion came away. This suggested the possibility that the secretion might be in another cell more distant from the main antrum.

THACKER NEVILLE suggested that the antrum was actually a reservoir for the right frontal sinus. He would disregard the X-ray report and look at the frontal sinus. He would be prepared to make a small incision through the eyebrow.

C. de W. GIBB (in reply) said that this patient had again been submitted to X-ray examination, and by a different radiologist, and the skiagram had shown only an opacity of the right antrum. He had hesitated to reopen the antrum because he wanted to convince himself that this pus was not coming from another sinus. He had no evidence of another sinus being the cause. The two skiagrams of the frontal sinus had revealed nothing.

**Traumatic Laryngeal Stenosis treated by Skin Grafting.—C. GILL-CAREY.**

John W., aged 11. On 16.7.37 ran into a wall (while riding a bicycle), striking his neck. He was admitted cyanosed and dyspnoeic. An immediate tracheotomy was performed.

13.8.37: Severe dyspnoea occurred on removal of the tracheotomy tube. Laryngoscopy showed marked stenosis of the larynx; no passage for a small bougie was possible.

13.10.37: Laryngofissure. Scar tissue removed. Skin-graft applied on a stent mould, which was kept in position for six weeks, when the larynx was allowed to close.

**Early Post-Cricoid Carcinoma.—R. SCOTT STEVENSON.**

A married woman, aged 76, complained of persistent difficulty in swallowing for the past two months. Laryngoscopic examination shows a smooth, pink swelling of the anterior lip of the oesophagus, extending towards the inter-arytenoid area of the larynx. The patient—a rheumatic old lady—refused oesophagoscopy examination.

X-ray examination (Professor Woodburn Morison): "Barium swallow: Barium passed normally down the pharynx into the oesophagus and there was no obstruction. In subsequent films, however, the lower part of the larynx and upper part of the trachea appeared to be pushed slightly forwards by a soft tissue swelling at the level of the 6th cervical vertebra; the margins are smooth, but the appearances suggest an early post-cricoid carcinoma."

The case is shown as evidence of the value of radiograms (in addition to the usual barium swallow examination of the pharynx and oesophagus) in the diagnosis of early post-cricoid carcinoma, and also to discuss treatment. It is intended to have high-voltage X-ray therapy carried out, in preference to radium bomb or surgery.

*Discussion.*—E. MUSGRAVE WOODMAN asked what was the best method of treatment in this type of case. It would be valuable to have some indication. He had found no good at all from deep X-ray therapy. He had carried out excision in two cases, one of which was successful, and he had on many occasions adopted a method recently advocated by Souttar—but practised in his clinic many years ago—of isolating the lower part of the pharynx, and inserting radium, so as to surround the tube with a plaque held in position by stent. That had proved in his experience a valuable method, but he was desirous of learning the opinions of others. Failing excision, the method of insertion of radium so as to surround the tube had been followed in his clinic.

G. EWART MARTIN said that he agreed with Mr. Woodman. During the last eighteen months every case of carcinoma of the pharynx under his care had been treated by deep X-ray therapy. This had been mainly on the suggestion of the radiologist, who wished to give every trial possible to heavy voltage X-ray therapy. In not one case had deep X-ray therapy given permanently satisfactory results, and no case had survived. His own view was that excision whenever possible was the best form of treatment. Possibly a 3 or 4 gr. radium bomb might be more effective than deep X-ray therapy.

E. BROUGHTON BARNES said that at a previous meeting of the Section Mr. Watt had shown three cases of post-cricoid carcinoma treated by deep X-rays. He believed that one of those patients had had the treatment three and a half years before the meeting. On examination nothing abnormal could be seen except that the mucosa was pale.

His (the speaker's) impression was that the result with deep X-ray treatment depended largely on the radiologist himself. If the radiologist began the treatment and left it to the radiographer to continue, he did not get the same results as those of the man who throughout personally concerned himself with the actual application of the X-rays.

It was of great importance that the radiation through the six ports of entry should cross on the growth. This implied careful localization and precise aiming.

A. LOWNDES YATES said that a few years ago a discussion had taken place<sup>1</sup> on the best method of treatment for these cases, and ten patients were shown who had been living for

<sup>1</sup> *Proceedings*, 1932, 25, 431.

more than two years after the beginning of treatment. Five of these had been treated by surgery and five by radiation.

S. C. SUGGIT referred to a patient, a woman aged 40, whom he had first seen at the end of 1933, requiring urgent gastrostomy. Subsequently she was treated for forty-five gram-hours with a one-gram unit of radium. She had left hospital quite well with the gastrostomy closed, and had afterwards married. She returned again, and another forty-seven and a half gram-hours treatment was given. He then lost sight of her altogether until quite recently, when he found that she was still living, after four years, and had had no further treatment since that time.

ERIC WATSON-WILLIAMS said that the general experience was that, whatever might be forthcoming in the future in the way of improvement, at present, radiation gave poor results. Whenever he had a favourable case he always advised the patient to consent to operation. He could not say that he had secured a lasting success. The specimen he was showing was from a patient who had died with symptoms of pneumonia on the fourth day following the first stage of oesophagectomy: this was a perfectly operable case from the technical point of view.

One problem was how to preserve the recurrent laryngeal nerves. It was easy to inflict fatal injury by damaging one or both of these just behind the cricoid. The growth had almost to be shaved off these nerves, and this was technically the most difficult part of the operation.

R. SCOTT STEVENSON said that he had seen three of his patients operated on for this condition during the last three years. They had lived only for a few months afterwards, and they had had such a miserable time that he was adverse to the idea of this patient undergoing lateral pharyngotomy, and therefore he was proposing to have high-voltage X-ray therapy carried out.

#### Web Stretching across Vocal Cords.—R. G. MACBETH.

Mr. I. I., aged 30, seen in November 1937, complaining of discomfort at the back of the nose and throat, and huskiness. The latter he had had all his life, and the former was a recent symptom following on a heavy cold. His larynx had been examined in 1914 by a laryngologist, who told his mother that there was a web across the vocal cords, and advised no active treatment. There was no history of any acute laryngeal disease.

*Condition on examination.*—There is a general congestion of the nose and post-nasal space, but no evidence of any active sinus infection. In the larynx there is a semilunar fibrous web stretching across the anterior third of the vocal cords. The voice is husky, but clear, and sufficiently loud for the patient's clerical occupation. He is not anxious for any surgical intervention.

*Discussion.*—C. A. B. HORSFORD recommended Mr. Macbeth to carry out operation. Both vocal cords were mobile and opposed perfectly, so that there would be no fear of adhesion or scarring with lack of a good voice in the future, and excision would be easy. The case recalled another in which a similar webbing had appeared as the result of a trauma—in fact attempted suicide—in which patient, a woman, did not cut right through the larynx, and a large fibrous web had appeared. After operation, although the patient was always short of breath, she acquired a voice. The cords were immobile, but the general health and breathing improved.

G. EWART MARTIN suggested that in this case the condition should be left entirely alone. There was no inconvenience at all, the man had no shortness of breath, he could carry on his work perfectly well, and his only difficulty was in speaking. He (the speaker) did not think that even if the cords were touched it would be possible to teach the patient—at his age—to speak any differently.

J. C. HOGG said that some years ago he had seen a similar condition in the larynx of a young man. An attempt was made to divide the web by means of diathermy. A fine electrode was used and the web was divided along one vocal cord only, allowing the rest to fall free. He had seen the patient two years later. The result was quite good; about nine-tenths of the divided web had disappeared and only a small amount was left. The voice, which had been very weak, became strong and serviceable.

## Section of Ophthalmology

President—W. H. McMULLEN, O.B.E., F.R.C.S.

[December 10, 1937]

### CLINICAL MEETING HELD AT THE WESTERN OPHTHALMIC HOSPITAL, LONDON

#### Osteoma of the Orbit.—E. A. BLAKE PRITCHARD, M.D.

P. E. J., male, aged 26. First seen March 1934. Twelve months earlier he had noticed a pricking feeling in the left eye, and six months later, progressive impairment of vision began in the same eye. During the previous six months there had occasionally been severe pain around the left orbit, maximal in the neighbourhood of the eyebrow. The patient complained of recurrent nasal catarrh, with obstruction of the left nostril. He made no other complaint with regard to his health. In 1930 he had had twelve months' antisyphilitic treatment at the London Hospital.

*On examination* (March 1934).—The left eye was proptosed; an attempt to push it backwards into the orbit met with firm resistance. No oedema or engorgement of the conjunctiva. Left pupil larger than right; showed no reaction on direct illumination, but reacted briskly on illumination of the right eye. Left fundus normal, apart from pallor of the optic disc. Visual acuity: Right eye,  $\frac{6}{6}$ ; left eye, perception of light only. External ocular movements full in right eye; slight reduction of lateral movement in left eye. Findings on neurological examination otherwise normal. Blood-Wassermann reaction negative. Skiagram of skull showed large, densely opaque mass, mainly to left of mid-line, obliterating sella turcica on lateral view and encroaching on back of orbit.

Patient admitted to University College Hospital. During the following three weeks there was rapid diminution of visual acuity in the right eye—down to  $\frac{6}{30}$ —without local restriction of the right visual field. A right frontal decompression was carried out. The right optic nerve was found to be much flattened and stretched around the side of a bony mass. An attempt was made to relieve the tension in the nerve by cutting away some of the tumour. When next tested, the patient was found to have no perception of light in either eye. Since the end of 1934 he has continued to have recurrent pains in the left side of forehead and the left eye has become progressively more proptosed.

Stereoscopic skiagrams, repeated in December 1937, show a great increase in the size of the tumour, but still, in spite of the almost complete dislocation of the eyeball out of the orbit, the external ocular movements of the left eye remain of considerable range.

#### Tumour of Sphenoidal Region with External Ocular Palsies.—E. A. BLAKE PRITCHARD, M.D.

Mrs. R. V., aged 67. Apart from symptoms of a gastric ulcer for which she was treated at St. Mary's Hospital 40 years ago, she had been consistently healthy until October 1937 when she noticed an increasing dimness of vision in her left eye. She attended the Western Ophthalmic Hospital under the care of Mr. Rugg-Gunn, and a small cyst was removed from the left lower eyelid. One week later a painful

swelling of both eyelids rapidly developed, with pain and numbness on the left side of the forehead and further rapid deterioration of visual acuity in the left eye. The swelling of the eyelids gradually subsided but the upper lid remained completely ptosed, and four weeks later visual acuity had been reduced to perception of light. She continued to complain of occasional aching pains in the left eyeball and in the left frontal region.

*Condition on examination* (8.12.37).—A well-nourished woman of good colour; signs of nervous abnormality confined entirely to the left side of the face. The left eye is completely covered by the closed eyelid, and the patient is unable to uncover it to any degree. When the upper eyelid is raised the eye is found to be rotated a few degrees laterally; there is no proptosis. Pupil slightly irregular; about 4 mm. in diameter; under homatropine it dilates gradually to 6 mm.; no contraction on attempted convergence. Optic disc pale; retinal vessels normal. No perception of light with left eye. No upward, inward, or downward, movement of this eye but a jerky and uncertain lateral deviation through a further 15 or 20 degrees. Corneal response on left side lost; sensibility to light touch and to pin-prick impaired on left side of forehead over area of distribution of left supraorbital nerve. Right eye shows healthy optic disc and retinal vessels, and visual acuity is  $\frac{1}{6}$ . The pupil is 3 mm. in diameter and reacts briskly on illumination. The external ocular movements are full and well sustained and the corneal response is brisk.

A lateral skiagram of the skull shows an area of irregular calcification on the left side, just in front of the left posterior clinoid process, and a further appearance which suggests that the lesser wing of the sphenoid is being eroded. An antero-posterior skiagram shows a slightly enlarged and irregular optic foramen on the left side.

**POSTSCRIPT.**—Since the date of the meeting, this patient has been admitted to hospital under the care of Mr. Wilfred Trotter, who explored the left side of the head and found a large, probably extradural, tumour mass lying at the back of the left orbit.

#### Myasthenic Weakness of the Extra-Ocular Muscles.—E. A. BLAKE PRITCHARD, M.D.

Mrs. A. S., aged 46. Had been in excellent health; no visual disturbance before June 1937, when she noticed difficulty in keeping her eyes open. During the following month left-sided ptosis developed and was noticeably worse towards the end of each day. In August 1937, following an accidental fall in the street, the ptosis became complete, but there were no other ocular symptoms. During the next two months, without specific treatment, the ptosis diminished, but at the end of October it again gradually increased.

*Condition on examination* (3.11.37).—A well-nourished woman; no signs of general ill-health. Cerebrospinal fluid, skiagram of skull, and full blood-count, all normal. Visual acuity, with correction: Right  $\frac{6}{12}$ ; left  $\frac{6}{18}$ . Right corneal scar; bilateral lens opacities; visual fields completely full to 1 mm. white object. Fundi: Normal discs and retinal vessels. Palpebral apertures narrowed, particularly on the left; this narrowing increases during the day and is invariably worse in the evenings. It is absent for a few minutes after the patient wakes from sleep.

External ocular movements: Right eye, normal lateral rotation, diminished upward and downward movement, and absent nasal rotation. Left eye, normal lateral rotation, diminished upward, downward, and nasal, rotation.

Cranial nerves otherwise normal. No weakness of palate, tongue, or facial muscles. No difficulty with chewing or swallowing and no impairment of phonation even after prolonged conversation. Skeletal musculature shows no wasting and no weakness of voluntary movement is developed after repetitive contraction of any

muscle. Tendon reflexes are brisk throughout and superficial reflexes normal. There is no impairment of sensibility, superficial or deep. Blood-pressure 150/72. Urine shows no chemical abnormality.

After the subcutaneous injection of 2 mgm. of prostigmine, the ptosis almost completely disappeared and the external ocular movements were markedly strengthened. Slight but steady improvement was observed under treatment with ephedrine and glycine.

This patient is to be regarded as suffering from a myasthenic weakness of the external ocular muscles and of the eyelids, not associated with any difficulty in swallowing or in phonation, or with any weakness of the orbicularis oculi.

#### **Tuberculous Periostitis of the Orbit, probably secondary to Tuberculoma of the Iris.—A. RUGG-GUNN, F.R.C.S.**

Mrs. L. C., aged 43, attended the Western Ophthalmic Hospital under another surgeon fourteen years ago, suffering from episcleritis of the left eye. Posterior synechiae were present in both eyes. Treatment included injections of tuberculin.

First seen by me early in 1933. A discrete nodule, judged to be tuberculous, was present on the anterior surface of the right iris near the ciliary margin at 6 o'clock. There was a slight projection of the corneo-scleral junction overlying the nodule. The Wassermann reaction (blood) was negative.

The patient was treated by injections of gold (sanocrysin 1 centigramme weekly). After four injections the nodule was perceptibly less in size and ultimately it disappeared. Shortly afterwards a cyst developed at the same place; this grew rapidly in size and was clear on transillumination.

Late in 1933, as the cyst was still enlarging and the eye was free from signs of active inflammation, the portion of iris containing the cyst was excised. This was followed in a few days by an inflammatory reaction, with profuse keratitis punctata, rise of tension, and ciliary injection. In spite of treatment the eye became worse and later was excised.

Two years later a series of tough confluent swellings appeared on the upper and inner orbital margins of the same side. These protruded into and involved the socket and the upper eyelid. At one point in the upper lid there was a small area of caseation. No evidence of bony involvement was shown by X-rays. The patient was examined at my request by Mr. Gordon Bryan, who kindly saw her twice and who agreed with the provisional diagnosis of tuberculous periostitis. The caseous area did not, in the end, perforate the skin, but regressed, and it has now disappeared. Probably the present condition consists of organized scar-tissue on the way to new bone formation.

On pathological examination neither the eye nor the cyst revealed conclusive evidence of tuberculosis, but the presence in both of endothelioid cells was reported.

It might be argued that the state of the eye after the iridectomy was not tuberculous inflammation but a sympathetic ophthalmitis; the pathological report would be consistent with either. On the other hand, repeated examinations of the left eye revealed no signs of sympathizing inflammation.

#### **Amaurosis after Gastric Hæmorrhage.—A. RUGG-GUNN, F.R.C.S.**

S. A., male, aged 47, was admitted to the Central Middlesex General Hospital on 12.11.37, following melæna of some days' duration and, on the day before admission, vomiting of a small quantity of bright red blood. He gave a history of indigestion extending over twenty years.

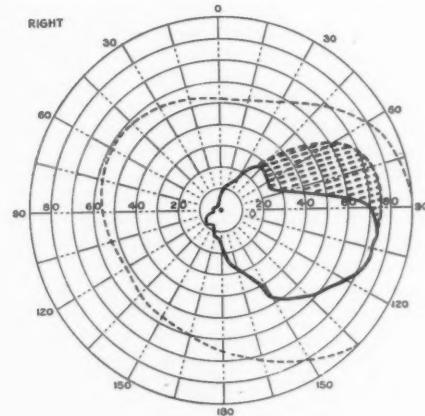
The patient was very pale. Blood-pressure 105/40; R.B.C. 1,300,000; Hb. 26%; C.I. 0.98. No further hæmatemesis or melæna after admission.

The pulse fell continuously, and on 14.11.37 the patient complained of dimness

of vision in the right eye. The right pupil reacted sluggishly to light. On 15.11.37 the right disc had a blurred outline. On 18.11.37 a transfusion of 350 c.c. citrated blood was given. Two days later another transfusion (400 c.c. citrated blood) was given. The right pupil did not react, directly or consensually, and there was no perception of light. The left pupil reacted well. There was slight papilloedema of both discs, right more than left. The retinal arteries were narrowed, and the patient complained of dimness of vision of the left eye, for the first time, i.e. twelve days after the haematemesis. Hb. 46%; blood-pressure 110/60. Next day the left pupillary reaction to light was lost and the patient was blind. Since then R.B.C. count has risen to 3,500,000, and Hb. to 70%; C.I. 1, and there has been no further hemorrhage from the gastro-intestinal tract. The amaurosis, however, has remained complete, although the patient has occasional hallucinations of sight.

I have notes of two other cases:—

(1) R. L., male, aged 23, an officer in a foreign Navy, had several gastric hemorrhages at sea. Details are lacking, but he is reported to have had four blood transfusions. Both pupils react to light. The left eye has no perception of light, but with the right eye there is an area of eccentric vision (v. chart, which is misleading in that the field appears to include the macula, owing to eccentric fixation). There is advanced optic atrophy in both eyes. Both



R. L. 1·5° white eccentric fixation.

fundi, throughout their extent, have a light spotted appearance, especially in the macular areas. Streaks of retinal pigment, which in places form an open network, radiate from the discs along the vessels in both fundi. The left eye is blind, but there is a temporal field in the right eye, extending from near the fixation point to about 70°, with an indeterminate area just above. With a Zeiss prism telescope he reads J 2.

(2) Mrs. U. Z., aged 18, suffered from metrorrhagia ever since the onset of menstruation. Ultimately, the menstrual function was abolished by the application of radium. Seen soon after a very severe uterine hemorrhage, she showed great pallor and complained of blindness which had developed twenty-four hours earlier. The discs were very white and the arteries narrow. The fundus which was naturally deeply pigmented, was rather grey in colour. Both pupils reacted slightly to light. Later, central vision improved to R. 1/8 and L., perception of light. The right field was contracted, especially on the nasal side.

These cases are rather rare. Eight or nine years ago Mr. E. F. Whiting described five cases, and two years ago Mr. E. Wolff suggested a rather attractive theory respecting the cause of the amaurosis, suggesting that the condition may be due to arterial spasm consequent on a diminished oxygen supply. The slight papilloedema seen in some cases must be a pressure phenomenon caused by fluid transudation into the optic nerve sheath, i.e. a reactive oedema such as often follows failure of the blood supply to a part. It is also curious that in the great majority of the published cases the sources of the bleeding have been the stomach or the uterus.

I am indebted to Dr. H. Carter, Medical Superintendent of the Central Middlesex General Hospital, and to Dr. Joules, the Physician-in-Charge, for permission to publish the first case.

Mr. E. F. WHITING said it seemed clear that when patients had had their constitution seriously depleted by repeated haemorrhages it was important to recognize the danger of optic atrophy occurring and, if possible, to keep the haemoglobin at not less than 50%.

**Bilateral Operation for Ptosis; Blaskovics' Method.**—R. LINDSAY REA, F.R.C.S.

The ptosis was first noticed when the patient was aged 18 (fig. 1). It gradually increased until, at the age of 50, she found it difficult to raise her eyelids



FIG. 1.—Before operation. Note the attempt of the frontalis muscle to elevate the eyelids, as shown by the distance between the eyebrows and the eyelids.



FIG. 2.—After operation. Compare with fig. 1. The eyebrows have assumed their proper level. The cornea are cleared from the overhanging lids.

sufficiently to uncover the pupils.

**Operation.**—The technique followed was that described by Professor Blaskovics in the *Archives of Ophthalmology*, 1929, n.s. 1, 672.

Figure 4 explains the anatomical rearrangement brought about. The cut

end of the levator attaches itself to the cut surface of the tarsal plate. The operation consists of splitting the upper eyelid into its three component parts—skin, muscle and conjunctiva. By pulling down and cutting off the redundant end of the



FIG. 3.—After operation. Showing normal power of completely closing the eyes.

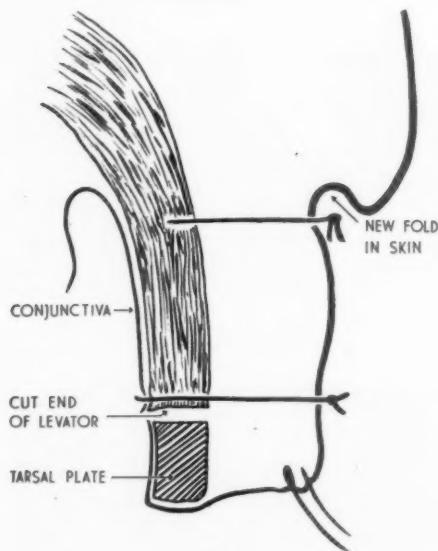


FIG. 4.

levator the conjunctiva and skin are slipped upwards, hence the entire shortening of the lid.

A similar operation was devised by Bowman, but Blaskovics' technique is better, particularly with regard to the formation of the new skin fold.

Mr. J. FOSTER said that before he used this method he had communicated with Professor Blaskovics, as it seemed to him that with the exception of an extra row of sutures designed to produce a new fold in the skin of the lid, this was Bowman's operation in a new guise.

Professor Blaskovics, in a personal communication, had confirmed his (the speaker's) opinion that the operation was suitable for every kind of ptosis, not excluding those with a congenital origin, in which there was a fibrous band instead of a levator. The effect of this band was such that the eyelid was put in a much better position. It was assumed, of course, that cases of paralytic ptosis in which exposure of the pupil would produce diplopia, were excluded. The importance of this was that all the classifications, which divided ptosis into various types, with various operations required for each, were now rendered pointless—as this one operation would serve for all.

He (Mr. Foster) had performed this operation in two cases, and would re-enforce Professor Blaskovics' own observation, that the immediate result, owing to œdema and other causes, was a little disappointing, but that improvement went on for at least eight months.

**Mature Cataract and Endothelial Web-Membrane in Anterior Chamber.—**  
H. H. SKEOCH, F.R.C.S.

I. H., male, aged 52.

*History.*—Failure of vision and squint of right eye for six months. States that when 8 years old he was struck a direct blow on the right eye with a stick. The eye was tied up for months but the patient could see with it subsequently till about six months ago when his right vision began to fail and the eye was noticed to squint outwards.

R.V. : P.L., light projection accurate ; L.V.  $\frac{1}{2}$ . Pupils active and equal, tension normal.

*Right eye.*—Corneal nebula. Old pigmented keratitis punctata. Endothelial web-membrane in anterior chamber adherent to post-corneal surface at ends and free in centre in anterior chamber. Pupil dilates fully with mydriatic, no synechiae. Mature cataract obscuring view of fundus. Deviates outwards, accurate light projection.

*Left eye.*—Cornea clear ; anterior chamber clear. Lens shows blue dot coronary cataract on dilatation ; media otherwise clear. Fundus normal.

The condition is probably the result of the old injury to the eye.

**Recurrent Tumour of Upper Lid.—**J. COLE MARSHALL, F.R.C.S.

Mrs. H., aged 61, first seen in October 1934. Movable, semi-solid tumour in outer third of upper lid ; diagnosed as dermoid or lachrymal-gland tumour. As the swelling did not become smaller it was operated on in March 1935. An encapsulated tumour adherent to cartilage, but not involving it, was removed.

First pathological report : "Granuloma : not a malignant growth." A second opinion did not agree ; it was that the growth was malignant, probably from the salivary-gland group, regarded by some authorities as carcinoma of the lachrymal gland. The pathologist's advice, however, was against drastic treatment.

For several months there were no signs of recurrence, but later on in the year, fullness appeared in the inner third of the lid and it was decided to remove the new growth. This was found to extend to the outer surface of the ethmoid. Pathological report, December 1935 : "A granuloma, not a true growth."

After this, it looked as if the entire upper lid was free from growth, but in the early spring of 1936, a fullness appeared in the upper fornix. The eye was pushed downwards and inwards ; vision—originally  $\frac{1}{2}$ —was down to  $\frac{1}{8}$ . There was some papillitis, and keratitis was beginning to appear in the upper third of the cornea. Various opinions were taken, the majority favouring the diagnosis of a new growth.

In September 1936 permission was given to remove the growth, but not the eye. A large tumour was shelled out ; it extended to the apex of the orbit and was lying against the periosteum of the outer wall, much in the position of the orbital portion

of the lachrymal gland. Recovery was uneventful : vision returned to  $\frac{6}{9}$ , and there was no sign of recurrence in October 1937.

Pathological report of tumour removed at the third operation : " Though usually cellular, this may well be of the type of ' mixed tumour of a salivary gland ' . If a complete removal has been made, I should consider that no further treatment is necessary."

**Two Cases showing the Use of Electrolysis in Localization.**—STEWART MACKY, D.O.M.S.

I.—B. H., male, aged 12. First seen 16.12.36. Defect had been noticed for two weeks.

*On examination.*—Retina freely detached in lower half with disinsertion at 7.30 o'clock, and a "hole" near the macula. Low retinal detachment upwards and inwards, flat in upper and outer quadrant. Long bands of choroiditis at 3 o'clock and 9 o'clock.

14.1.37 : Combined Larsson and Safar operation from 8.30 o'clock to 3.30 o'clock with division of inferior rectus. Nearly all the detached portion went back except that around the macula. The appearance of a hole remained, surrounded by vessels, apparently raised.

Vision =  $\frac{6}{36}$ , but subsequently I came to think that the patient had been cheating me about his vision. Appearances remained much the same, with a little more flattening around the macular hole.

7.7.37 : Fell into swimming-bath ; detachment recurred. Colleagues agreed that the hole at the macula showed real parallax, and as scarring around the old disinsertion seemed very firm, the macular hole was attacked in the hope of retaining some field.

29.7.37 : Operation. External rectus divided and macular region explored. Taking the insertion of the inferior oblique as a guide (as Mr. Cole Marshall has suggested) the position of the macula was marked on the sclera and verified by electrolysis puncture, and direct observation by ophthalmoscope. The macula was surrounded by Safar punctures. By mischance, the long ciliary artery was divided during separation of adhesions ; this may have something to do with the excessive reaction.

The retina has become reattached nasally, but there is a portion towards 8 o'clock that is now assuming the appearance of retinitis proliferans ; at first this had seemed more obviously to be a detachment. There is, of course, no central vision.

II.—R. G., male, aged 28. First seen 26.5.37.

*History.*—The patient was plugging a ceiling in February 1937 when the right eye was hit by a fragment. Both the lid and the eye bled, and a blister formed on the inner corner of the right eyeball.

*On examination.*—Small scleral scar at 2 o'clock about 4 mm. from limbus. Dark mass projecting into vitreous about 2 D.D. from the ora at 4 o'clock.

28.5.37 X-ray report : Metallic foreign body 12 mm. above central corneal axis, 8 mm. nasal to central corneal axis. 13 mm. deep to anterior surface of cornea.

4.6.37 : *Operation.*—Sclera exposed and marked  $16\frac{1}{2}$  mm. from limbus. Electrolytic puncture. Direct observation showed bubbles 0.5 D.D. behind mass. Sclera incised accordingly, and foreign body exactly exposed. Haemorrhage into vitreous is clearing very slowly. V.,  $\frac{1}{2}$ .

## Section of Surgery

President—G. GREY TURNER, M.S.

[January 5, 1938]

### On Certain Features of Gangrene of the Legs

By J. F. PHILIP, Ch.M.

THE skiagrams shown were obtained from amputated legs by injecting into the popliteal artery a special barium emulsion of such a consistence that, while it filled the smaller arterioles, it did not permeate to the venous system. The emulsion was injected by an apparatus so designed that the fluid was introduced at a constant pressure, equivalent to the patient's systolic blood-pressure before operation. In each case dissection of the limb proved that the appearances presented by the



FIG. 1.—A patient aged 36. The larger arteries show clearly delineated walls, and there exists a free collateral circulation.

skiagrams were to be relied on as giving a fairly accurate picture of the obstructive element in the arterial tree.

*The circulation in normal lower extremities.*—The appearances presented after injection of the arterial tree at different age-periods are indicated in figs. 1 and 2.



FIG. 2.—A patient, aged 70, whose systolic blood-pressure was 100 mm. Hg. A contrast with fig. 1 is provided by irregularity in the wall of the popliteal artery and the extreme degree of narrowing of the beginning of the anterior tibial artery. This patient had no sign of gangrene.



FIG. 3.—A patient, aged 83; the affected leg was at first cold, white, and painful; later it became mottled. An arterial circulation is not demonstrable beyond the calf.



FIG. 4.—Dilatation of vascular spaces in the media. (Hæmatoxylin and eosin.)  $\times 98$ .

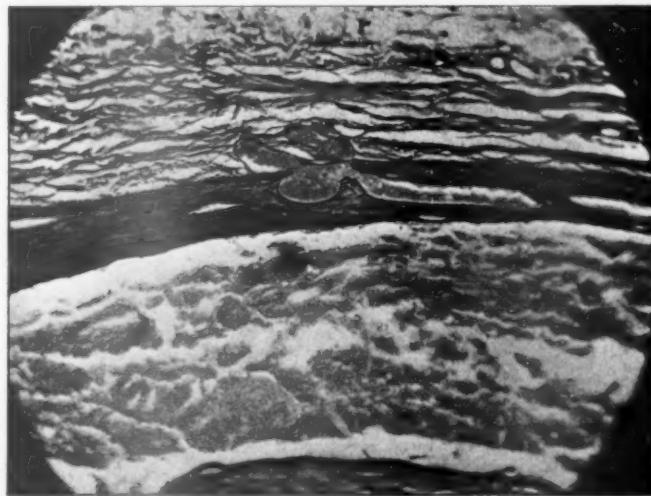


FIG. 5.—To show continuity between the vasa vasorum and the medial channels. (Hæmatoxylin and eosin.)  $\times 98$ .

*The circulation in gangrene.*—Gangrene in arteriosclerosis: An example of the arterial circulation in gangrene due to arteriosclerosis is shown in fig. 3. There are three types of vascular lesion occurring in this form: (1) The circulation is not demonstrable beyond the calf; (2) the brunt of the process falls on the popliteal artery, its bifurcation, and the beginning of its terminal branches, while the remainder of the arterial tree is spared to some extent, and (3) the lesion affects the whole arterial tree in an almost uniform manner.

Clinically, in the second type, rubor is marked in the dependent limb, whereas in the third type rubor does not develop whatever the position of the limb, which remains cold, painful, and waxy.

The success of any attempt to revascularize a limb showing evidence of arterial insufficiency depends on several factors which may modify the typical histological features of arteriosclerosis.



FIG. 6.—A complex channel, a new artery in the organized thrombus. There are muscle-fibres in its wall. (van Gieson's stain.)  $\times 98$ .

These are: (a) The development and utilization of collateral vessels; (b) the appearance of small vascular chinks in the media, and the enlargement of these (fig. 4). Serial sections have proved that continuity exists between these channels and the *vasa vasorum* (fig. 5); this is a new observation; (c) with the advent of thrombosis, two additional routes appear (i) simple endothelial-lined tunnels, inactive conduits through the block, and (ii) complex channels through the thrombus, which are complete vessels. I say "complete", advisedly, because they have all the components of a new artery, for they contain muscle-fibres and elastic tissue in their walls (fig. 6). Serially cut sections from arteriosclerotic limbs have failed to

demonstrate any definite continuity between the *vasa vasorum* and this type of vessel, but in a section of the digital artery from a case of Raynaud's disease (fig. 7) a new artery is present within the old one, and it is directly continuous with another



FIG. 7.—Digital artery from a case of Raynaud's disease. There is a new artery within the old, and it communicates with one of the *vasa vasorum*. (Haematoxylin and eosin.)



FIG. 8.—A patient, aged 49. Although gangrene involved the anterior half of the foot, the collateral circulation is good.

vessel outside the main artery. This arrangement has not hitherto been described, and, with the medial chinks, provides an alternative path of considerable importance.

Gangrene in diabetes : Three clinical forms of gangrene occur in diabetes.  
(1) The gangrene is dry, superficial in character, and affects pressure points. The

presence of pulsation in the major arteries of the leg, and a normal or relatively high surface temperature, as measured by a thermocouple, indicate a free circulation. Such patients complain bitterly of rest pain, and the gangrene, which usually yields to conservative treatment, is associated with toxic neuritis. (2) The gangrene is due to arteriosclerosis. This form is divided into two clinical groups : (a) in which the arteriosclerosis is of mild degree, and (b) in which the arteriosclerosis is severe. In the former group conservative measures usually prevail, but in the latter the clinical features, pathology, and treatment, are those of arteriosclerotic gangrene occurring apart from diabetes. (3) The gangrene is a purely cellulitic process, and may be extensive, although the circulation in the limbs is good. The primary cause of gangrene in such cases is the presence of infection in devitalized tissue. A low amputation, or even local surgical measures are sometimes successful here, provided the arteriosclerotic element is negligible. Each of the three forms of gangrene can exist by itself, but the combination of arteriosclerosis and infection is frequent, and modifies the treatment.

**Gangrene in thrombo-angiitis obliterans** : In this disease an excellent collateral circulation is the rule, even in the presence of extensive superficial gangrene. This is more especially the case before the patient reaches the age of 50, and it sometimes happens that the gangrenous limb is the warmer of the two. These facts, the toxic appearance of such patients, and the focal and diffuse collections of round cells which occur in association with the vessels, favour the assumption of a toxic or infective origin of the disease. Skiagrams show that long segments of the large arteries are occluded (fig. 8), and the degree to which a collateral circulation can exist in the presence of gangrene involving the anterior half of the foot, is revealed by the same figure. In patients over 50, arteriosclerosis modifies the clinical and pathological picture. From a consideration of the skiagrams and histology in this disease, I believe that no single line of attack can be universally successful, and that physiotherapy, sympathectomy, and amputation each has its place.

It remains only to add that the veins are seldom occluded in arteriosclerosis ; in diabetes they tend to show patchy intimal thickening and thrombosis is a frequent occurrence, while in thrombo-angiitis obliterans they appear to be equally affected with the arteries.

### Cardiac Complications of Major Abdominal Surgery

By PAUL WOOD, M.B., M.R.C.P.

THIS paper is not based on any special investigation but is merely an expression of experience gained from the clinical study of post-operative cases which have developed symptoms suggesting heart-trouble to the surgeon. Such cases include a wide variety of clinical entities, and I have therefore considered them according to their presenting symptoms. I have not included complications directly due to the anaesthetic—such as sudden death under chloroform.

#### PAIN IN THE CHEST

Post-operative myocardial infarction may occur for two reasons. Firstly, in patients with stenosis of the coronary ostia from syphilitic aortitis, or with severe occlusive coronary atherosclerosis, a considerable drop in blood-pressure may so interfere with proper coronary filling that myocardial infarction results without coronary thrombosis. A previous history of angina pectoris is usual in such cases. Secondly, post-operative thrombosis may occur in an atheromatous coronary vessel for reasons similar to those given for the occurrence of post-operative venous thrombosis. The first type may occur soon after the operation when the blood-pressure may be low, or as a further complication of dehydration, haemorrhage, and collapse ;

the second occurs later, during the second week, as does post-operative venous thrombosis.

The pain of myocardial infarction is substernal. It may radiate upwards into the throat, neck, jaw, and face, and down the inner side of the arm to the ring and little fingers, on either or both sides. Rarely it may be epigastric. The pain is not located over the apex-beat or in the left-breast region. Its character is often constricting and always constant. This constancy is important, being quite unlike the pains of colic, pleurisy, and fibrositis. The severity of the pain varies from a mild ache or numb sensation to the most excruciating agony, and its duration is commonly measured in hours.

Associated symptoms include faintness, weakness, collapse, sweating, dyspnoea, nausea, and vomiting—but all these may be absent. The shock is succeeded by a mild rise of temperature which rarely lasts longer than three days. Leucocytosis is equally transient. Abnormalities of rhythm such as paroxysmal ventricular tachycardia, paroxysmal auricular fibrillation or flutter, and any form of heart-block or nodal rhythm, are significant. A fleeting pericardial friction rub is heard in about 10% of cases. Subsequent systemic embolism may unmask the nature of the accident.

Serial studies on the blood-pressure, the erythrocyte sedimentation rate, and on the electrocardiogram will usually provide diagnostic evidence. The initial drop of blood-pressure is usually followed by a low pressure maintained for several days, after which recovery is slow. The initial pressure may or may not be regained. The sedimentation rate usually remains normal for a day or two; it then rises to reach a maximum in about ten days or even later. The return to normal is slow and usually occupies several weeks.

Finally, it must be stressed that in cases of myocardial infarction, clinical examination of the heart often reveals nothing abnormal. Its occurrence is common in people with previously unsuspected heart disease. On the other hand the patient should be carefully questioned as to previous angina pectoris, however slight.

*Primary pericarditis* has been described as a post-operative complication by Butsch (1937) from the Mayo Clinic. This may be difficult to distinguish from myocardial infarction complicated by pericarditis. There are, however, several points of difference.

The pain of pericarditis (Capps, 1932) (the condition is usually painless) is either due to pleural involvement, in which case it has the characteristics of pleural pain, or it is phrenic pain and may be referred to the anterior border of the left trapezius in the neck. The maximum pain may be substernal or slightly to the left of the sternum. The friction rub of primary pericarditis usually lasts several days, whereas the rub following myocardial infarction is commonly fleeting. The blood-pressure does not drop in primary pericarditis unless it is complicated by shock or unless there is effusion with tamponade. Finally, the electrocardiogram, though showing similar qualitative S-T changes in both conditions, is distinctive, in that in pericarditis the changes are most marked in lead 2 (Wood, 1937), whereas in myocardial infarction they are most marked in leads 1 or 3.

The third type of chest pain related to the cardiovascular system is that following pulmonary embolism, which will be considered later.

The majority of post-operative chest pains are not cardiac and may be due to pleurisy, intercostal fibrosis, tracheitis, or to subphrenic conditions involving the gall-bladder, the pancreas, the stomach, or the peritoneum. Cholecystitis, acute pancreatitis, and perforated duodenal ulcer have all been mistaken for myocardial infarction.

#### DYSPNEA

Post-operative dyspnoea is commonly due to pulmonary collapse, to bronchitis, or to bronchopneumonia. A distended abdomen may so elevate the diaphragm as to cause dyspnoea, from reduction of the vital capacity of the lungs. Uræmia must

be borne in mind, and air-hunger may result from haemorrhage. But if to dyspnoea is added one other symptom or sign suggesting heart trouble the case is usually diagnosed incorrectly as one of heart failure. I have known this other sign to consist of a few ectopic beats. If there is a trace of oedema in the feet the diagnosis may not be questioned, even though there may be extensive varicosities, or known anaemia, or obvious malnutrition, or marked obesity. Yet heart failure is rare after operations. Even seriously diseased hearts behave surprisingly well. One has seen patients with myocardial infarction operated upon for gall-stones with no ill-result. Many patients with severe hypertensive heart disease stand cholecystectomy extraordinarily well. I hope I shall be forgiven when I say that when things go wrong the surgeon is sometimes too apt to blame the heart. It is true that the heart must stop before the patient is legitimately dead, but it is also true that he does not die because of his heart unless he dies from cardiac syncope or from congestive heart failure.

Now cardiac syncope results from ventricular standstill, from ventricular fibrillation, from too-rapid a heart-rate, from sudden block of a valve orifice or a main arterial trunk from thrombus, and occasionally from too weak a cardiac contraction. It is a rare event apart from sudden death. There are only two post-operative causes which are at all likely—myocardial infarction and pulmonary embolism.

Dyspnoea at rest, if cardiac, means congestive heart failure, and this means serious organic heart disease. It is most unlikely that this will have escaped previous recognition. The most drastic surgery will not induce a healthy heart to fail, and the enforced rest both before and after operations protects the diseased heart.

When congestive heart failure occurs it should be easily recognized. There are two types depending on whether the congestion is confined to the pulmonary circuit or whether it is systemic. The former results from left ventricular failure and occurs especially in hypertensive heart disease and in aortic valvular disease; the latter results from right ventricular failure and occurs especially in mitral stenosis, in *cor pulmonale*, and as an end-result of left ventricular failure.

Left ventricular failure gives rise to dyspnoea, orthopnoea, paroxysmal cardiac dyspnoea, and to pulmonary oedema. The findings include evidence of considerable left ventricular enlargement from hypertension or from aortic valvular disease, bilateral basal pulmonary râles, gallop rhythm, and pulsus alternans. Myocardial infarction may produce the same clinical picture with far less cardiac enlargement. The electrocardiogram is invariably abnormal and the pulmonary circulation time considerably prolonged.

The diagnosis of right ventricular failure is made primarily upon the recognition of engorged pulsating cervical veins. Enlargement and tenderness of the liver may be difficult to detect, on account of the abdominal wound, and dropsy is a less certain sign. The diagnosis of congestive heart failure is more accurate when attention is paid rather to the neck than to the legs. The patient should be propped up at about 45 degrees and the neck inspected. At this angle venous pulsation above the clavicular level means right ventricular failure. If the veins are dilated, but do not pulsate, there is mechanical venous obstruction. Oedema alone is no evidence of heart failure. These are simple and well-known facts, yet they are only too frequently ignored.

Dyspnoea of sudden onset may be due to acute left ventricular failure, to massive collapse of the lung, or to pulmonary embolism. The first of these, as I have already indicated, is rare as a post-operative complication; the second should be recognized by the physical signs. The third deserves special mention.

#### PULMONARY EMBOLISM

I believe that the clinical manifestations of pulmonary embolism are not sufficiently appreciated. Pain in the chest and haemoptysis are but two common symptoms which in no way cover the clinical picture. The diagnosis is often difficult.

Post-operative venous thrombosis occurs during the second week, commonly about the tenth day, and usually commences in the veins of the pelvis or of the legs. Varicose veins, previous thrombophlebitis, obesity, polycythaemia, and congestive heart failure predispose to the condition. The surgical lesion itself may initiate the process. Post-operative factors include the rise in platelet count, which reaches a maximum about the tenth day, dehydration, sufficient to increase the blood viscosity, and the sluggish venous return from the lower half of the body which results from a combination of posture, immobility, shallow breathing, and tight abdominal binders. In my experience pulmonary embolism is more common following childbirth, gynaecological operations, fractures of the lower extremities, herniotomy, and appendicectomy, than after upper abdominal operations. This may indicate the importance of the local factor.

The clinical phenomena which may be produced by pulmonary embolism include :—

(1) Sudden death. (2) Sudden collapse with extreme dyspnoea. (3) Symptoms simulating those of myocardial infarction. (4) Transient substernal tightness and dyspnoea. (5) Pulmonary infarction with fever, pleural pain, and haemoptysis, or there may be no subjective manifestations of any kind.

Occasionally patients may present themselves with a complication of pulmonary embolism. These are : Right ventricular failure with engorged cervical veins ; paradoxical embolism ; pleural effusion, which may or may not be haemorrhagic.

*Sudden death.*—It is often said that when a patient calls for the bed-pan and then falls back dead the diagnosis is pulmonary embolism. It has even been stated that the sensation produced by dislodgment of the clot in the pelvis gives rise to the desire to open the bowels. This is a fallacy. Patients may call for the pan before falling back dead when they die from coronary thrombosis or from ventricular fibrillation. The explanation is not clear. However, if sudden and unexpected death occurs a week or so after operation, the most likely cause is pulmonary embolism.

*Sudden collapse with extreme dyspnoea.*—At least two-thirds of the pulmonary circulation must be blocked before serious symptoms arise. This means that emboli causing collapse must lodge at the bifurcation of the main pulmonary artery and straddle the carina. They are here subjected to powerful and changing forces of pressure and blood-flow, which may shift them onwards into the left or right pulmonary artery where they again straddle the first bifurcation. Here they are likely to pack. Blood may force its way round them so that pulmonary infarction may not occur. On the other hand pieces of the embolus may break off and, passing onwards down the pulmonary arterial tree, may block a smaller vessel and produce infarction. The main embolus, after being packed against the sides of the vessel, becomes organized.

The syndrome produced by these large emboli consists of sudden collapse with extreme dyspnoea, and may be followed by a most dramatic recovery. The following case illustrates this type :—

*Case I.*—Mrs. E. L., aged 74. The patient was admitted to the Hammersmith Hospital at 12.40 a.m., October 31, 1937, with a fracture of the neck of the left femur. She was in fair condition. A portable X-ray film was taken at 2.30 p.m. on the same day. Ten minutes later she suddenly collapsed, became very breathless and cyanosed, vomited profusely, and almost lost consciousness. She noticed, however, a great "banging" of her heart. She was thought to be dying, but to the surprise of witnesses she rallied after some minutes, her colour improved until she became quite flushed, dyspnoea disappeared and the pulse improved in volume. At 7 p.m. the blood-pressure was 110/70 and the pulse-rate 95.

I saw her the following day when she was feeling well again ; the blood-pressure was 150/70 and the pulse normal. There were no abnormal physical signs in the heart or lungs, and there was no occult blood in the faeces. An electrocardiogram showed a simple inversion of T 3.

The diagnosis was almost certainly pulmonary embolism, but there was no subsequent pulmonary infarction, and there was no haemoptysis or pleural pain. The embolus may have lodged at the bifurcation of the main pulmonary artery and have been subsequently packed to the side.

*Symptoms simulating those of myocardial infarction.*—Large pulmonary emboli, sufficiently big to cause dyspnea and collapse, are sometimes accompanied by substernal pain. When this happens the diagnosis has to be made from myocardial infarction, and this may be very difficult. The description of the attack itself may be identical in the two conditions. The clinical findings may not differ. The electrocardiogram may show similar changes if the myocardial infarction is of the T 3 type. There are three points which may help. First, which is the more likely? If the accident occurred on the tenth day after herniotomy in a young person with no previous history of angina the diagnosis would not be in doubt. In an elderly male who gave a previous history of angina pectoris, however slight, myocardial infarction would be more probable. Secondly, the degree of dyspnoea is greater in pulmonary embolism and may be associated with acute right ventricular failure, with engorgement of systemic veins, whereas in myocardial infarction extreme dyspnoea is usually due to acute left ventricular failure with pulmonary oedema. Thirdly, if there is much elevation of the S-T origin in lead 3 in the electrocardiogram the diagnosis will be myocardial infarction. (Pulmonary embolism never produces S-T changes in lead 1.)

The following case illustrates the difficulty of diagnosis:—

*Case II.*—Mrs. A. R., aged 68. This woman was being treated by rest in bed for hypertensive heart disease. Her blood-pressure was 260/150, and it fell with rest to 180/110. She had never had angina. The usual investigations were carried out and nothing unusual was found.

On February 6, 1936, a severe substernal pain developed and lasted throughout the night. Her colour was grey, there was moderate dyspnoea, and the pulse was small and rapid. There was no syncope, no nausea, no vomiting, and but little sweating. I saw her the following morning, when her temperature was 100° F., pulse-rate 110, and blood-pressure 100/65. Pain was still present but was less severe. There was a slight cough and the sputum was a little blood-stained. There were bilateral basal pulmonary râles but she had had these before. They may have been more extensive. There were no other abnormal clinical findings. A white count showed a rise to 14,000 per c.mm., her erythrocyte sedimentation-rate had risen to 50 in one hour by the Westergren method, and an electrocardiogram showed changes suggestive of posterior basal myocardial infarction. This appeared to be the diagnosis and she was treated as such.

Subsequent events seemed to confirm the diagnosis. The pain disappeared completely in a few days, the signs in the chest remained the same, the cough continued, but there was no further blood in the sputum, the temperature returned to normal on the third day, the white count on the fourth day, and the pulse-rate during the second week. The sedimentation rate continued to rise during the second week and reached a maximum of 100 on the sixteenth day. The blood-pressure remained relatively low for three weeks, after which it slowly climbed back to a maximum of 160/90. Serial electrocardiograms showed changes compatible with posterior basal myocardial infarction.

The patient never regained her strength and slowly became drowsy and confused. She developed weakness of the right arm, and finally anuria, and died quietly on April 1, nearly two months after the accident. The blood-urea shortly before death was 49 mgm. %.

Autopsy revealed an organized pulmonary embolus with shrinkage and re-establishment of the pulmonary circulation. There was an old thrombosis of the right iliac vein, and a recent one of the left ovarian vein. There was moderate hypertensive heart disease, but the coronary vessels were healthy.

The case illustrates a condition produced by pulmonary embolism almost indistinguishable from myocardial infarction.

*Sudden substernal tightness and dyspnoea.*—It must be remembered that more than 60% of the blood-flow through the pulmonary artery must be obstructed before serious embarrassment to the circulation can take place. The serious cases, therefore, result from lodgment of the embolus at the bifurcation of the main pulmonary artery, or from more than one embolus. A large embolus may lodge at the bifurcation of the left or right branch of the pulmonary artery and cause no immediate symptoms,

apart from sudden transient tightness of the chest and dyspnoea. These symptoms may never be mentioned by the patient unless special inquiry is made.

The true onset of this type of pulmonary embolism is well illustrated in the following cases:—

*Case III (Chart I).*—R.W., a woman aged 59, had had a gynaecological repair performed on February 3, 1936. She was convalescing satisfactorily when on the eleventh day she had a sudden attack of substernal tightness and dyspnoea, but it was quite transient and she did not mention it at the time. On the following day a sudden pain developed in the right side of the chest when she breathed. The temperature rose abruptly to  $102.5^{\circ}$  and the pulse-rate to 110. Haemoptysis and consolidation at the right base followed. On February 22, eight days after the first embolism when her condition had greatly improved, she had a second attack of dyspnoea, this time with collapse. She was shocked, cyanosed, sweating, and in much distress, but had no pain. The pulse-rate was 140 and the blood-pressure was too low to be recorded. Three days later, pain developed suddenly in the left chest—and caught her

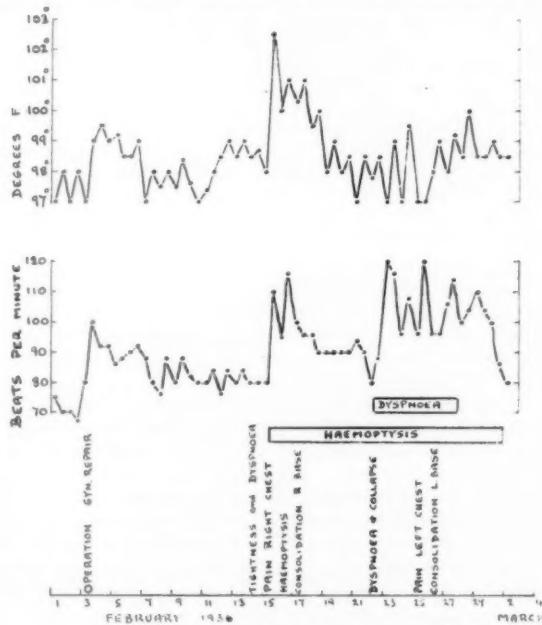


CHART I.—R. W. Post-operative pulmonary embolism.

on breathing, and the following day consolidation appeared at the left base. Haemoptysis continued throughout. There was obviously another pulmonary embolism. On both occasions tightness and dyspnoea preceded the pleural pain by at least twenty-four hours.

*Case IV (Chart II).*—Winifred L. This case is interesting in that it illustrates the sudden onset of pain in the chest fifteen minutes after removal of abdominal sutures, on the tenth day after operation (she had had a subtotal hysterectomy and right ovariectomy). The pain was transient. A few hours later a second attack of pain occurred and was associated with dyspnoea and sweating. This second pain was of characteristic pleural type. The following day consolidation was found at the right base and haemoptysis followed. Six days later there was a moderate amount of fluid at the right base. The temperature which had risen abruptly to  $101.5^{\circ}$ , continued so for about a week; dyspnoea lasted four days; and haemoptysis lasted a week. The patient made a complete recovery.

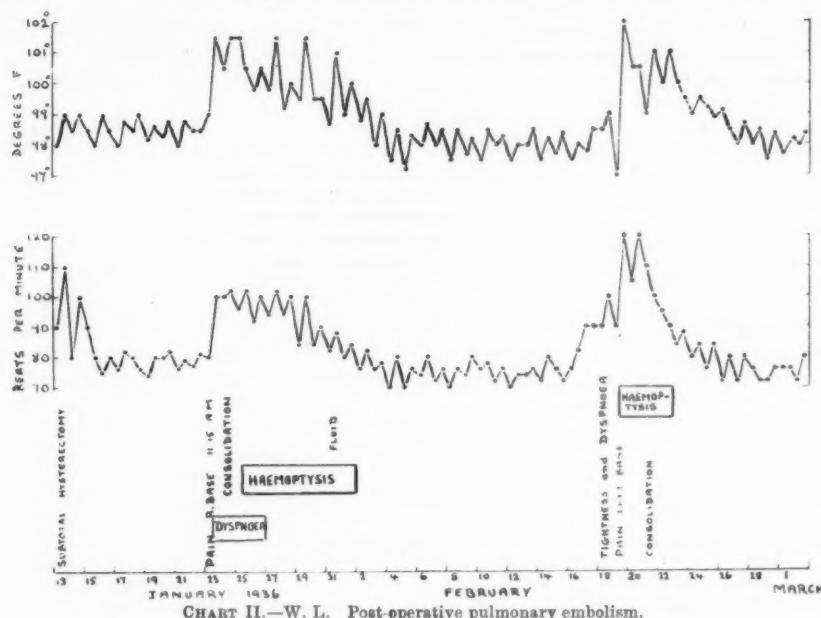


CHART II.—W. L. Post-operative pulmonary embolism.

Twenty-six days after the accident she had a sudden attack of tightness and dyspnoea but did not mention it. The following day she had a left pleural pain preceded by haemoptysis. Two days later she developed consolidation at the left base. The chart shows the associated rise of temperature and pulse-rate.

This second attack shows that haemoptysis may precede the pain. It should be evident that lodgment of the embolus gives rise to sudden collapse if large enough, to tightness and dyspnoea if a little smaller, and to no symptoms at all if smaller still. If the embolus is not packed to the side of the vessel, pulmonary infarction follows and may give rise to haemoptysis and to pleurisy, and the pleurisy may be followed by effusion. If the embolus is packed to the side of the vessel so that complete occlusion does not take place, organization and shrinkage of the embolus occurs, the circulation is re-established, and infarction does not follow. Of course a part of the thrombus may break off and, passing distally, may produce a small infarction.

These two cases also illustrate the classical symptoms of fever, haemoptysis, and pain—the fifth syndrome mentioned above and dependent upon pulmonary infarction.

The sixth type of pulmonary embolism is silent and is found at autopsy. Small infarctions may be present without haemoptysis and without pleural pain. This type may be compared with the silent emboli of small systemic arteries.

#### COLLAPSE

Sudden collapse may be due to myocardial infarction or to pulmonary embolism, and is usually associated with pain or with dyspnoea. The following case of sudden collapse without other symptoms is interesting and was difficult to diagnose clinically.

*Case V.*—Richard L., aged 64, had a gastro-enterostomy performed on February 9, 1937. There was a large ulcer of the lesser curvature and a duodenal ulcer close to the pylorus,

causing obstruction. There was no evidence of malignancy. Pre-operative investigations revealed atherosclerosis, a small longitudinal heart, a blood-pressure of 105/65 and considerable wasting.

The post-operative course was uneventful until February 28, when, at 11 p.m., the patient suddenly lost consciousness. The actual attack was unassociated with any other symptoms and lasted only a few seconds, but he remained very faint for half an hour. On examination he was found to have an almost imperceptible pulse and a blood-pressure of 70/40. There was no pain, no dyspnoea, no sweating, no nausea or vomiting, no abdominal sensation or any other significant symptom or finding. An enema was given and no blood was found in the faeces.

During the night he felt very ill and still a little faint. Next morning he retched once and brought up a little clear fluid. I saw him at 6 p.m. He was a little better, but still felt weak. The pulse-rate was 68 and regular; the blood-pressure was 70/50, and he looked pale. The heart sounds were almost inaudible, but there was emphysema; there was no pericardial friction. I was rather at a loss as to diagnosis, and considered that the complete absence of pain and dyspnoea ruled out myocardial infarction or pulmonary embolism. It was thought that the attack might have been vaso-vagal, and that there was still marked vagal over-activity. The asthenic condition with naturally low blood-pressure and slight anaemia were looked upon as aggravating factors. Ephedrine  $\frac{1}{2}$  gr. t.d.s. was advised. An electrocardiogram was taken and was developed immediately. To my surprise it showed a classical myocardial infarction. The advice as to ephedrine was promptly cancelled and the patient was re-examined for sensory loss. It was then found that he had anaesthesia to pin-prick over the chest from the level of the 2nd to the 9th rib, and Dr. Purdon Martin, who saw him later, thought that this was probably due to tabes dorsalis, but there was no other evidence and the Wassermann and Kahn reactions were negative. The following day the W.B.C. count had risen to 22,000 with 84% of polymorphonuclears. There was no pyrexia. Serial electrocardiograms followed the usual course.

The case illustrates the syncopal type of myocardial infarction occurring on the fourteenth post-operative day.

Collapse of slower onset is usually heralded by tachycardia and a falling blood-pressure. These two complications will therefore be considered together.

Auricular flutter and paroxysmal tachycardia occasionally occur after operations, but the usual causes of a rapid regular pulse and a falling blood-pressure are dehydration, infection, and haemorrhage. Marriott and Kekwick (1937) have recently stressed the importance of preventing and treating dehydration. They rightly state that any patient—not continuously mouth-breathing or under the influence of drugs of the atropine group—who has a dry mouth is dehydrated. Thirst must be treated before more serious symptoms develop. What is the good of injecting coramine, cardiazol, and other curious remedies when the patient simply needs water? The demonstration of dehydration by electrocardiography is an equally curious procedure. The pulse-rate may be 160 or even higher in severe cases, and the physician is expected to diagnose paroxysmal tachycardia; but he does not do so, and everybody is disappointed except the patient, who knows nothing about it and asks for another drink of water. The proper technique for fluid administration is described very thoroughly by Marriott and Kekwick (1937), and I will only say here that if the intravenous route is used 3,600 c.c. may be given in twenty-four hours, and that if the rectal route is employed double this amount can be given. Such large quantities can only be retained with Murphy's technique.

Haemorrhage is another cause of a very rapid pulse-rate and especially so when combined with dehydration. It must be remembered that after a large haemorrhage, rapid recovery of blood volume can only take place at the expense of tissue fluid, and if this is already depleted a serious state of affairs arises. The blood volume remains below normal, tachycardia may be extreme and—most important of all, because it masks the correct diagnosis—the blood-count and haemoglobin value may not be much altered. An electrocardiogram is usually asked for in these cases, to rule out

paroxysmal tachycardia, but an estimation of the blood volume would give more useful information, though the need for fluids should be obvious.

Infection—especially pneumonia and peritonitis—is the third great cause of tachycardia, and this only too frequently occurs in patients who have had a severe haemorrhage. Unfortunately pneumonia may cause a true paroxysmal rhythm change, either auricular fibrillation, auricular flutter, or paroxysmal tachycardia, and therefore one must be willing to take an electrocardiogram in all cases of unexplained post-operative tachycardia, although the reward is meagre.

Early recognition of dehydration and of pulmonary infection saves much worry and many lives.

*Irregularities of rhythm.*—Occasional ectopic beats are easily recognized and are of no significance. They are exceedingly common. When, however, the pulse is irregularly irregular the diagnosis is not always easy. When this irregularity appears during the post-operative course the likely diagnosis is multiple auricular ectopic beats especially if the patient is elderly and has a respiratory infection. An electrocardiogram is essential to distinguish this form of rhythm from auricular fibrillation.

All forms of ectopic beats may be produced by almost any infection or intoxication, by gastric distension, and by a variety of other causes. They do not of themselves point to heart disease. They are usually transient and need no special treatment, but if they are persistent, quinidine may effect their departure.

If auricular fibrillation is present the patient should be overhauled by a physician, and medical treatment instituted.

#### CONCLUSIONS

- (1) Significant cardiac complications are uncommon in major abdominal surgery.
- (2) The most dramatic events are usually due to pulmonary embolism, but myocardial infarction may occur.
- (3) Collapse of slower onset is rarely cardiac, but may be due to dehydration, to haemorrhage, to peritonitis and ileus, or to some other unsuspected complication.
- (4) Dyspnoea alone is more often pulmonary than cardiac.
- (5) Congestive heart failure is a rare event.
- (6) Abnormalities of rhythm are usually caused by ectopic beats and are not significant, but paroxysmal tachycardia, auricular flutter, and auricular fibrillation, may occur.
- (7) Finally, when faced with obscure post-operative disasters, the surgeon would do well to consider every other possible complication before accusing the heart. In the absence of an autopsy it is often difficult to convince the surgeon that the heart is innocent.

[I wish to thank Sir Frederick Menzies, Chief Medical Officer of the County of London, for his permission to publish this paper.]

#### REFERENCES

BUTSCH, W. L. (1937), *Proc. Staff. Meet., Mayo Clin.*, **12**, 737.  
 CAPP, J. A. (1932), "An experimental and clinical study of pain in the pleura, pericardium and peritoneum", New York: The Macmillan Co.  
 MARRIOTT, H. L., and KEKICK, A. (1937), *Practitioner*, **139**, 250.  
 WOOD, PAUL (1937), *Lancet* (ii), 796.

### Blood Transfusion at the Front

film by Dr. Frederic Duran-Jordá, Chief of the Spanish Government Blood-transfusion Service

Shown by R. W. B. ELLIS, M.D.

THE film shows the organization of a blood-transfusion service under conditions of modern warfare, and illustrates the Duran-Jordá method of storage and distribution of blood. In Barcelona, a panel of several thousand voluntary blood-donors has been established and classified, from which donors are called in rotation at intervals of

not less than three weeks. Special inquiry is made as to a previous history of malaria or other infection. The original appeal was primarily for Group 2A and universal donors.

Whilst the ideal would undoubtedly be the grouping of all soldiers on enlistment, and inclusion of their blood group on their identity disc, existing conditions necessitate two systems of transfusion : (1) Grouping of patient and use of blood from donor of the same group, where time and facilities permit ; (2) the use of blood from a universal donor without grouping the patient, under emergency conditions, as a first-aid measure. The greatest supply of blood has therefore to be from universal donors. During the present food shortage, donors are, when possible, given a tin of condensed milk when they supply blood.

In taking the blood, 15 c.c. of 4% sodium citrate solution is drawn into the flask by water-suction, followed by 300 c.c. of blood and a further 15 c.c. of citrate. Not more than 3 to 400 c.c. is taken from each donor ; 1 grm. glucose per litre is added. The blood is kept at 1° C. whilst it is examined bacteriologically, the Wassermann reaction completed, and the blood group checked. It is then filtered through a silk bag, and the bloods from six donors of the same group are mixed (it is found that this mixing lessens the danger of individual reactions). 300 c.c. are transferred by vacuum suction to a special container ("Auto-injectable Rapid"), which is filled with filtered air under a pressure of two atmospheres, and sealed. To the sealed end of the container is fitted a sterile filter, rubber tubing, Murphy drip, screw clamp, two-way faucet, and needle (the last being covered with a glass container). The apparatus is dated, labelled with the blood-group number, and boxed ready for transport. In the refrigerator it can be kept for at least eighteen days.

At the time of an offensive, requests for additional supplies of blood can be telephoned to headquarters, and supplies sent out by the blood-transfusion lorry. (More recently, an ambulance train has been fitted with refrigerators, &c., for the transport of blood). The interior of the lorry can be seen, containing a generator, two refrigerators, and room for two stretchers (fig. 1).



FIG. 1.—Interior of lorry, showing dynamo driven by petrol engine to maintain refrigeration of the blood.

Transfusion from a universal donor can be carried out in the field in a matter of seconds after standing the container in warm water ( $45^{\circ}\text{ C.}$ ) for twenty minutes.

*Use of apparatus* (fig. 2).—Keeping the screw-clip closed and the tap of the two-way faucet perpendicular, the container is set up in a vertical position (sealed end below), using the hook which may be hung from the button-hole of the operator. The seal of the container is broken by bending the rubber-tubing with which it is covered, the glass cover of the needle is removed (A), and by releasing the screw-clip the air is expelled from the apparatus by the blood which flows out under pressure. When the first drops of blood have been ejected, the screw clip is closed, and the two-way faucet turned. A 5- or 10-c.c. syringe is attached to (B). The vein is

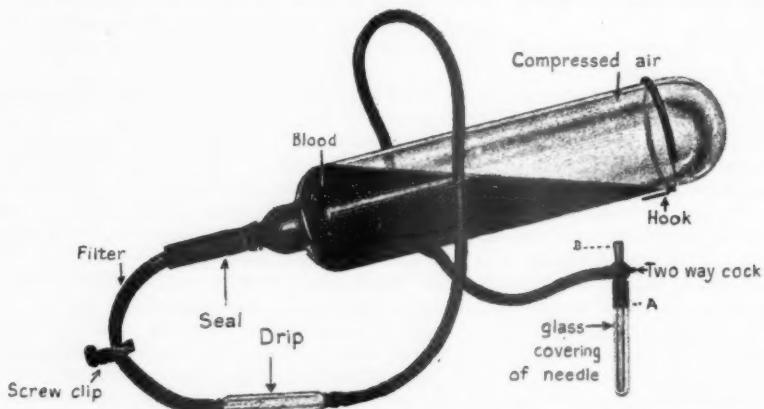


FIG. 2.—“Auto-injectable Rapid” transfusion apparatus. (Laboratorio Quimico-Biologico Pelayo, Barcelona.)

punctured, and a small amount of blood is withdrawn from it into the syringe in order to assure the correct position of the needle. The faucet is again turned so that the blood in the container can flow through the needle. The screw clip is gradually released, and used to control the rate of flow. The clip must be closed immediately the blood has left the container, and the needle withdrawn.

The method of preparation and storage of blood in the “Auto-injectable Rapid” container has three main advantages in war-time:—

- (1) Large supplies of blood can be immediately available at the time of an offensive.
- (2) Injection can be carried out extremely rapidly in the field.
- (3) The simplification of the method makes it possible for transfusion to be carried out by partially trained auxiliaries as a first-aid procedure.

## Section of Surgery

### SUB-SECTION OF PROCTOLOGY

President—J. P. LOCKHART-MUMMERY, F.R.C.S.

[February 9, 1938]

**Plastic Operation for Traumatic Anal Atresia.**—Sir CHARLES GORDON-WATSON, K.B.E., F.R.C.S., and Sir HAROLD GILLIES, C.B.E., F.R.C.S. M. D. H., aged 11 (at operation).

*History.*—When a baby, 3 days old, the buttocks and perineum were severely burnt by a hot-water bottle and the infant nearly died. Healing was followed by severe constriction of the anus and loss of control and power of voluntary defaecation. The bowels were opened with enemas. On several occasions just previous to operation there was a severe hold-up in the colon and large masses were subsequently evacuated by copious enemas. The abdomen was always distended.

*Condition before operation.*—Extensive scarring in the perineum, pin-point anus drawn downwards to same level as ischial tuberosities. Abdomen distended.

*Operations.*—(1) May 13, 1935: Laparotomy. Colon very much dilated and hypertrophied (megacolon). Colostomy.

(2) May 31, 1935: Plastic operation (Sir Harold Gillies). Incision round the anus through all layers of the scar. As the knife cut through to the fatty layer the scar tissue receded on each side to a considerable distance, laterally and posteriorly. When further scar tissue had been excised round the anal margin, the anus contracted and assumed a natural position. The raw area thus produced on each buttock was about 4 in.  $\times$  5 in. Two large skin grafts were taken from the thigh and lightly sown into position. Long ends of the sutures were tied over sponge-gauze pressure. The grafts were satisfactory.

July 29, 1935: Colostomy closed.

August 15, 1935: Patient returned home. Rectum functioning normally.

February 1938: Perfectly well; rectum functions normally.

[Mr. Rainsford Mowlem deputized for Sir Harold Gillies and described the skin graft in detail.]

**Recurrent Lymphoma of the Rectum.**—Sir CHARLES GORDON-WATSON, K.B.E., F.R.C.S.

The patient, a woman aged 50, was operated on by the late Mr. W. S. Perrin in July 1934 for a small rectal tumour which was considered to be an adenoma and was removed by local measures.

Dr. H. Scott-Wilson reported that the pathological appearances were those of a gumma.

In November 1937, when the patient was under the care of Dr. Geoffrey Thompson of Scarborough, a tumour similar to the original one was discovered. She was seen by Mr. Braithwaite, of Leeds, who referred her to me. I found a smooth oval sessile tumour in the anterior wall of the rectum, about  $2\frac{1}{2}$  in. from the anal margin, with a smooth surface but ill-defined edges. The mucosa was quite normal but was adherent to the tumour, which could not be pulled away from the muscular wall. I excised the tumour, together with the overlying mucosa, which was closely adherent to it, by diathermy, and sutured the margins together. The wound healed by first intention.

Dr. Dukes made the following report (1.1.38): "Microscopic examination shows the tumour to be a lymphoma. The growth affects a somewhat extensive area and it is rather ill-defined at its margins, so there is a possibility that it may recur, although there is no sign of malignancy."

*Remarks.*—These tumours are rare. At St. Mark's Hospital only 10 cases have been met with during the last ten years. Dr. Dukes reported details of three cases before this Sub-Section in March 1934.<sup>1</sup> These cases have been followed up and so far no recurrence has been met with. Clinically the tumours may be mistaken for adenomata, and in the absence of microscopic examination a correct diagnosis may be missed. The fact that normal mucosa overlies the tumour should prevent this mistake.

The interest of this case lies in the fact that an innocent tumour has recurred and has ill-defined margins, though it shows no evidence of malignancy. The report on the original tumour emphasizes the difficulty of histological diagnosis in some cases as between a lymphoma and an inflammatory hyperplasia not easily diagnosed from a gumma.

#### Specimens shown by G. GREY TURNER, M.S.

(1) *Carcinoma of the rectum treated by perineal conservative resection with carcinoma of the hepatic flexure of the colon, both from the same patient.*

The man was aged 55 when the rectum was excised eighteen years ago. Twelve years later, he assumed that he was suffering from a recurrence, but the symptoms proved to be due to an independent growth in the hepatic flexure. This was excised, and an end-to-end anastomosis was carried out. The patient is now well and has perfect rectal function and control.

(2) *Carcinoma of the ampulla of the rectum treated by perineal conservative resection.*

The patient was a man aged 63, a victim of diabetes. The operation was carried out in two stages after a preliminary colostomy. Recovery was satisfactory, with complete restoration of rectal control.

Death occurred nine years later from diabetic gangrene, without any suggestion of recurrence of the carcinoma.

(3) *Cuff resection of the rectum for a non-malignant papilloma.*

The excised bowel has been turned inside out to better demonstrate the growth.

The patient was a man aged 64 at the time of the first operation. There was no preliminary colostomy. The wound healed in three weeks. The patient acquired perfect rectal function.

Death occurred six years later from nephritis and without bowel symptoms of any sort.

<sup>1</sup> *Proceedings*, 1931, 27, 925, Sect. Surg. (Sub-Sect. Proct.), 20.

(4) *Malignant growth in the first part of the rectum, which occurred twenty years after an old-fashioned perineal excision for the same disease.*

The patient was aged 50 at the time of the original operation and in the intervening years enjoyed good health except for the troubles associated with a stricture at the site of the muco-cutaneous anus. The symptoms, produced by the growth shown in the specimen, were attributed to a recurrence of the stricture, and their importance was not appreciated until late on in obstruction.

The death of the patient gave an opportunity for demonstrating that there was no general dissemination of the carcinoma.

(5) *Carcinoma of the transverse colon.*

The patient, a man aged 50, complained of the development of a tender swelling in the upper abdomen after an acute attack of pain. At operation the growth was found in the middle of the transverse colon; it was diffusely adherent over a wide area of parietal peritoneum. The exploration was followed by preliminary cæcostomy.

The patient improved rapidly and when the abdomen was reopened four weeks afterwards, the adhesions had largely disappeared. The bowel could be readily separated from the parietes, and resection and end-to-end anastomosis were straightforward. Recovery was uneventful, and the cæcostomy was closed six weeks later. A comparatively recent case.

**Four Cases of Double Carcinoma of the Rectum and Colon.—W. B. GABRIEL, M.S.**

(1) Mrs. N. R., aged 57, complained of rectal bleeding with abdominal colic after meals. Rectal and sigmoidoscopic examination revealed a small malignant ulcer, freely mobile, in the upper third of the rectum; it was not causing any obstruction, and the possibility of a second growth at a higher level was discussed.

*Operation* (April 1937).—Laparotomy revealed an operable carcinoma in the pelvic colon many inches above the rectal growth. Perineo-abdominal excision in one stage was carried out, the upper growth being exteriorized with an adequate margin. The patient made an excellent recovery and remains in good health.

*Pathological findings.*—The upper growth (pelvic colon) presented as a flat constricting tumour,  $1\frac{1}{2}$  in. in diameter; the lower (recto-sigmoid) growth was 8 in. lower down and was seen as a small raised ulcer  $\frac{1}{2}$  in. in diameter. Both tumours proved to be adenocarcinoma, grade 1. Two lymphatic glands behind each growth contained metastases (fig. 1) [C2 case].

(2) G. R., male, aged 73. A large ulcerated carcinoma of the rectum was seen at 5 in. from the anus.

*Operation.*—Preliminary laparotomy revealed a second carcinoma in the pelvic colon. Both tumours were removed by radical perineo-abdominal excision. Death from cardiorenal failure occurred on the seventh post-operative day.

*Pathological findings.*—The tumours proved to be adenocarcinoma, grade 3, with extensive lymphatic spread from each (fig. 2) [C2 case].

(3) Male, aged 68, reported a recent attack of abdominal pain and difficulty with the bowels, culminating in partial obstruction. He was a frail subject with a rapid pulse, and a distended cæcum could be felt contracting. Rectal examination revealed a circular carcinoma high up, a typical malignant edge being seen at 5 in. from the anus. While awaiting operation acute intestinal obstruction supervened; the cæcum presented visible and palpable peristalsis. The subsequent surgical operations were as follows:—

24.10.37 : Blind cæcostomy.

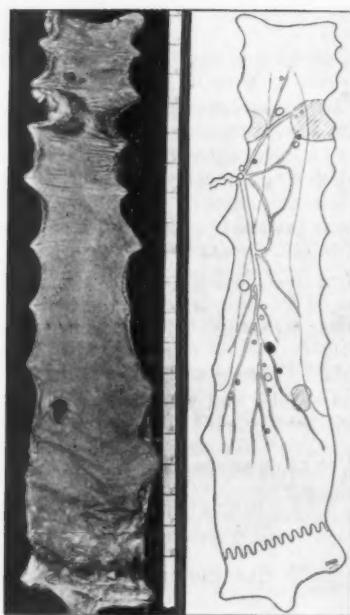


FIG. 1.—Operation specimen of double carcinoma of the rectum and pelvic colon, with chart of gland dissection.

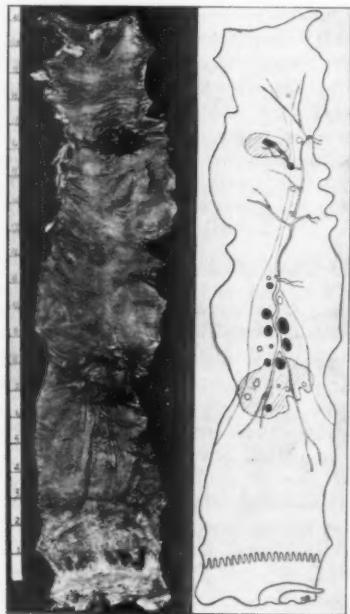


FIG. 2.—Operation specimen of double carcinoma of the rectum and pelvic colon, with chart of gland dissection.

10.11.37: Right paramedian laparotomy. A constricting carcinoma was found in the proximal part of the transverse colon, in addition to the rectal carcinoma, which could be felt at the peritoneal reflexion in the pelvis. The transverse colon tumour was mobilized and brought out for resection by Paul's method.

8.12.37: Perineal excision of the rectum and left iliac colostomy in one stage.

A month later the transverse colostomy was closed by suture under local anaesthesia, after preliminary crushing of the spur. The patient now has a functioning iliac colostomy.

*Pathological findings.*—The growth in the transverse colon proved to be an adenocarcinoma, grade 2, with extensive spread into the pericolic fat, but without glandular metastases. The rectal growth was an adenocarcinoma, grade 3, with one infected gland at the upper end of the specimen [C 2 case]. A separate nodule just above the ano-rectal line proved to be an atypical carcinoma composed of round or polygonal cells not secreting mucus. Both specimens showed evidence of extensive melanosis.

(4) M. L., male, aged 54, with an ulcerated fungating carcinoma in the upper third of the rectum.

*Operation (4.2.37).*—Laparotomy; liver and omentum free from palpable metastases; perineo-abdominal excision in one stage carried out. After operation some abdominal distension was noted, but it subsided and no further trouble took place till the thirty-sixth post-operative day, when abdominal colic developed, with vomiting and distension of the caecum. A further exploration seemed imperative.

*Second operation (12.3.37).*—Laparotomy revealed free fluid and gross distension of the caecum due to a "string" carcinoma in the middle of the transverse colon. A good deal of local infiltration appeared to have taken place, with adhesion to the mesentery of the small intestine. The growth was dissected free and removed by an exteriorizing operation; the colon distal to the growth was divided and closed, the growth then being brought outside the abdomen after ligation of the middle colic artery; a terminal colostomy at the hepatic flexure remained.

*Subsequent course.*—The patient recovered from this operation and was discharged home a month later, but rapid peritoneal and hepatic metastases developed, and he died a few days less than four months after the excision of the rectum.

*Pathological findings.*—The rectal growth, 2 in. in diameter, was a grade 2 adenocarcinoma, which was commencing to spread to the peri-rectal fat [B case].

The stenosing growth in the transverse colon was a grade 3 adenocarcinoma which had spread extensively into the pericolic fat, and metastases were present in one regional gland.

*Comment.*—In this case the growth in the transverse colon was missed at the original exploration, and it was clearly this growth, the more malignant of the two, which rapidly caused a fatal ending.

#### Diverticulitis of the Cæcum.—W. B. GABRIEL, M.S.

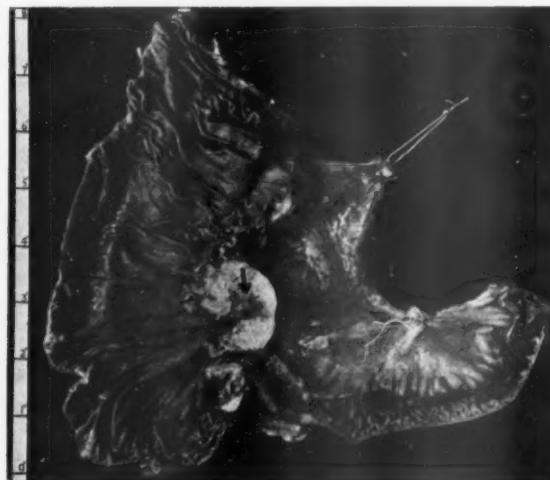
The patient, a single woman, aged 44, gave a history of pain in the right side of the abdomen of three days' duration, with many previous attacks. There had been no vomiting and the bowels had been opened regularly. Examination showed a small palpable tender mass in the right iliac fossa.

*Operation.*—Laparotomy (April 1937) revealed a hard mass involving the inner aspect of the cæcum ; it was indistinguishable from a carcinoma, and hard glands were palpable in the ileo-cecal angle. A right hemicolectomy was carried out in one stage, the ileum being anastomosed by a side-to-side junction to the transverse colon. The patient made an uninterrupted recovery.

*Pathologist's report* [Dr. Cuthbert Dukes] :

The specimen consisted of the cæcum, appendix, terminal 8 in. of the small intestine and a portion of the ascending colon. The cæcum was distended and its wall thickened along the mesial border, forming a hard tumour. Enlarged glands could be felt in the neighbouring mesentery. The appendix was thickened.

Dissection did not reveal any ulceration or definite tumour within the cæcum, but a large diverticulum about  $\frac{1}{2}$  in. in diameter was found in the mesial border, opening into the cæcum immediately above the ileo-cecal valve. This diverticulum was surrounded by a hard yellowish-white band of tissue (see fig.).



Internal appearance of cæcum and small intestine, one-third natural size, showing position of diverticulum (marked by arrow).

**Microscopic structure :** Microscopic examination shows the diverticulum to be lined with mucous membrane, normal in appearance except for some melanin pigmentation. The submucosa and muscle tissues surrounding the diverticulum are continuous with these coats in the cæcum, but densely infiltrated with inflammatory cells. Several small abscesses are present in the surroundings of the diverticulum and neighbouring connective tissue. The regional lymphatic glands show hyperplasia, congestion and inflammatory changes. There is no sign of neoplasm. The lesion is entirely inflammatory in origin, the cellular reaction being of the type found in infections with the pyogenic bacteria.

**Pathological diagnosis :** Diverticulum and abscess of cæcum.

### Endometrioma of the Pelvic Colon

By C. E. DUKES, M.D.

AN endometrioma or adenomyoma is a tumour composed of glandular tissue, stroma, and non-striped muscle. It occurs in the uterus as either a diffuse or a circumscribed growth. It derives its origin from the uterine mucosa which grows in the tumour in association with myomatous tissue.

When tissue resembling an endometrioma is met with outside the uterus the term endometriosis is used. For instance, the lining of chocolate or tarry cysts of the ovary may consist of tissue resembling endometrium, and it is thought that these represent implants of endometrial tissue carried along the fallopian tubes, the altered blood in the cyst representing menstrual haemorrhage. The rupture of a chocolate cyst sets free endometrial tissue which may settle in the recto-vaginal septum and give rise to an adenomyoma or endometrioma of the pelvic colon. Such tumours of the pelvic colon are rare. Most of the reported cases have been associated with chocolate or tarry cysts of the ovary, but, if the theory of implantation is correct, they might be expected also apart from ovarian cysts, being due to fragments of endometrium falling directly from the fallopian tubes into the pouch of Douglas. The case I am about to report was not associated with an ovarian cyst although the ovary was adherent to the tumour.

(1) *Case of endometrioma of the pelvic colon.*—The patient was a middle-aged woman who had been operated on by a gynaecologist on account of a tumour in the pelvis, which might have been a chocolate cyst of the ovary. At operation the left ovary was found to be adherent to the pelvic colon, but the ovary was small and, except for the adhesions, appeared to be normal. A careful search was made for any evidence of endometrioma in the uterus, ovaries, pouch of Douglas, recto-vaginal septum, and round ligaments, but since none was found it was concluded that the growth which could be felt in the sigmoid must be a separate tumour of the bowel and beyond the province of the gynaecologist. The case was therefore handed over to another surgeon as one of carcinoma of the pelvic colon, and the growth was excised by Paul's operation on May 25, 1937.

Microscopic examination of the operation specimen proved that the first diagnosis was correct and that the tumour in the pelvic colon was an endometrioma and not a carcinoma.

*Description of operation specimen.*—*Gross characters:* The specimen consisted of a portion of the pelvic colon 9 in. in length. At a distance of 1 in. from the distal end the lumen was obstructed by a mass of hard tissue situated in the wall of the colon and projecting inwards. Two other nodules forming round swellings projected into the lumen of the colon close by. There was no ulceration of the pelvic colon mucosa either over the tumour or elsewhere and no diverticula were found. The tumour appeared to be embedded in the muscle coats of the colon.

Dissection showed the largest nodule to be very dense and fibrous in consistence and without any clearly-defined boundary.

*Microscopic examination:* The tumour in the wall of the pelvic colon was composed of dense connective tissue and non-striped muscle. Embedded in this were several tubular glands lined by well-differentiated columnar epithelium and surrounded by a loose cellular connective tissue, the arrangement being that of an endometrioma.

This case is of interest to surgeons because it illustrates the difficulty of distinguishing between a carcinoma of the colon and an endometrioma. The gynaecologist decided that it must be a primary growth of the colon because there was no sign of any ovarian cyst.

(2) *Case of carcinoma simulating endometrioma*.—In this case a surgeon made a mistake in the opposite direction. In the course of an abdominal operation he discovered an ovarian cyst adherent to a tumour of the pelvic colon and removed the ovary and pelvic colon tumour under the impression that he was dealing with an endometrioma. However, it proved to be something different.

Examination of this operation specimen showed the ovary to be enlarged and cystic and adherent to the pelvic colon opposite to the intestinal tumour. Judged from its gross characters there was every reason to suppose that the intestinal growth was an endometrioma secondary to an endometrial cyst of the ovary, but microscopic examination showed both the ovary and intestinal tumour to be adenocarcinoma of the intestinal type.

The patient was a woman aged 39 who two years previously had suffered from carcinoma of the splenic flexure. This was removed and the pathological report recorded extension into the pericolic fat, and metastases in four of the six lymphatic glands examined. The ovarian cyst found at the second operation was a recurrence from this tumour of the splenic flexure and the growth in the pelvic colon was an extension—or one might say a return—of the tumour, from the ovary to its natural home in the intestine.

#### **Resection of the Sigmoid Flexure for Adenomatosis with Restoration of Bowel.—J. P. LOCKHART-MUMMERY, F.R.C.S.**

The patient, Miss Y., aged 35, had a severe haemorrhage from the rectum. A diagnosis of diffuse polyposis of the large bowel was made and a transverse colostomy was performed in January 1936 in the provinces. She came to see me in July 1937 with a view to the possibility of having the colostomy closed. An X-ray photograph showed considerable narrowing over about 5 in. of the pelvic colon and polyposis. In September 1937 I cut out the colostomy opening and sewed it up. After changing gloves, I excised the affected loop, which consisted of 22 in. of the transverse and descending, and part of the sigmoid, colon. The proximal end of the transverse colon was then sutured laterally to the stump of the sigmoid and the two ends were brought out as a colostomy. The patient was transfused at the end of the operation, which, however, she stood very well.

A few days after the operation a clamp was put on and the spur destroyed. All bowel external to the skin was then cut away with a diathermy knife and the patient was sent home. In January this year the faecal fistula was closed and the patient is now having normal actions of the bowel through the rectum.

The specimen shows adenomatosis of unusual type with considerable fibrosis of the bowel wall. There was no family history of the condition.

#### **Congenital Angioma of the Rectum and Sigmoid Flexure.—J. P. LOCKHART-MUMMERY, F.R.C.S.**

I first saw this patient, Mr. B., in September 1920, when he was aged 45. He had had serious haemorrhages at irregular intervals all his life and had on two occasions been operated on for piles under the mistaken belief that the bleeding was coming from internal haemorrhoids. Sigmoidoscopy revealed an enormous angioma beginning just above the middle of the rectum and extending upwards as far as could be seen with the sigmoidoscope. A great number of very large vessels were seen pulsating immediately under the mucous membrane. After careful consideration it was decided that nothing could be done to remedy the condition.

I saw the patient again in 1929 and 1934. He had from time to time had severe haemorrhages.

In November 1937 he came into the Clinic in London under my care, having chronic obstruction. He had been treated in the provinces with radium ; the radium container had shifted and a very bad burn on the anterior wall of the anus had resulted in a severe stricture, which was almost completely blocking the bowel.

A transverse colostomy was performed and the bowel was examined from the abdominal aspect. Fifteen inches of the rectum, sigmoid flexure, and descending colon, were involved in the angioma. The whole of this portion of the bowel was thickened and erectile and consisted of masses of large vessels, and the same condition was present in the mesentery. It was obvious that any attempt to excise the angioma would be extremely dangerous, owing to the large size of the feeding vessels, many of which were as thick as one's little finger. After the patient had recovered from the operation and the obstruction was removed, internal proctotomy was carried out. Alcohol was injected into the spine to try to control the pain which was very severe owing to the radium burn.

This is the twelfth case of this condition described in the literature. I had one case in a man aged 50, who died from haemorrhage in Paris, and two cases have been described by Dr. Bensaude (of Paris), who also collected fourteen cases from various sources. To the best of my knowledge no case has been successfully treated by excision or by any other means, and all the patients have eventually died of haemorrhage. My patient is now aged 63.

This curious condition must be very rare. The angioma may be either venous or arterial or—and, I think, most commonly—a mixture of both. In the case described above the growth was certainly in the main an arterial angioma and would justify the name cirsoid aneurysm of the colon. The affected part of the colon when examined from the abdomen is markedly erectile and pulsates in one's hand.

Any part of the rectum or colon may be affected and Bensaude has described a case affecting the small intestine.

#### Multiple Carcinomata and Familial Adenomatosis, treated by Perineo-abdominal Excision.—C. NAUNTON MORGAN, F.R.C.S.

H. M., male, aged 38, agricultural labourer.

*History.*—From the age of 15 this patient had had recurrent rectal bleeding, due to rectal polypi. In April 1937 he was admitted into a country hospital where several polypi, which were prolapsing through the rectum, were excised. On admission into St. Mark's Hospital he complained of recurrent bleeding and the passage of slime. He had no diarrhoea or constipation.

*Family history.*—Two uncles died of carcinoma of the rectum at an early age ; also one brother had a carcinoma of the rectum.

*On examination.*—The rectum was found to be full of semi-pedunculated and pedunculated polypi and a carcinoma could be felt in the ampulla on the right side. Sigmoidoscopy confirmed the presence of polypi and also of a small carcinoma. Biopsy confirmed the diagnosis of carcinoma.

*Operation (30.7.37).*—One-stage perineo-abdominal excision was carried out.

*Pathologist's report [Dr. Cuthbert Dukes] :*

*Gross characters :* The specimen consisted of the rectum and pelvic colon measuring 20 in. in length. The whole mucosal surface was covered by innumerable sessile and pedunculated adenomata. The larger of these were 2 in. in diameter. Three of the tumours were hard in consistence and semi-ulcerated. The position of these growths is marked by arrows in the accompanying photograph (fig. 1).

*Microscopic structure :* The three tumours whose position is marked on the photograph

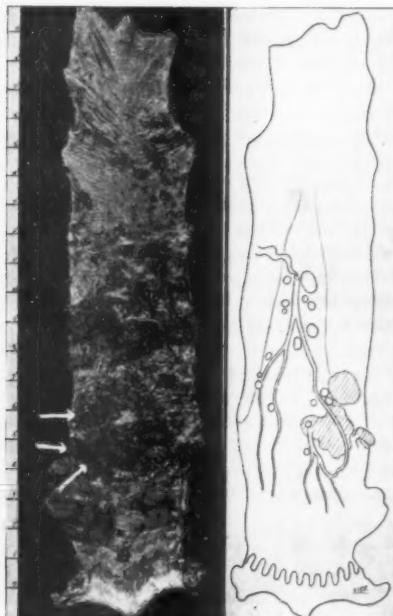


FIG. 1.—Familial adenomatosis and carcinomata of rectum (marked with arrows).

are? adenocarcinomas, fairly well differentiated in character. Histological malignancy Grade 1.

Methods of spread: (1) By direct continuity: The malignant growths had infiltrated the rectal wall but not spread to the extrarectal fat. (2) Venous spread: There is no evidence of this. (3) Lymphatic spread: The ano-rectal and haemorrhoidal glands were free from metastases. (17 glands examined (fig. 1).)

Classification: Multiple carcinoma of the rectum associated with polyposis intestini. Three separate malignant growths limited to the rectal wall. No lymphatic metastases [an A case].

**Recurrent Carcinoma of the Rectum following Conservative Resection, treated by Abdomino-perineal Excision.—C. NAUNTON MORGAN, F.R.C.S.**

A. S. B., female, aged 52; a trained nurse. This patient was seen in July 1936 complaining of constipation of three months' duration and the occasional passage of blood and slime.

*On examination.*—Nothing could be felt with the finger but on sigmoidoscopy, at 12 cm. from the anus, the lower edge of a carcinoma could be seen. This was confirmed by biopsy. The patient refused to have a permanent colostomy and therefore some method of conservative resection had to be considered.

*Operation* (July 1936).—An exploratory laparotomy was carried out and a carcinoma could be felt in the upper third of the rectum, its lower edge being about 1½ in. above the level of the peritoneal reflection in the pouch of Douglas. It appeared to be quite mobile and no glands could be felt. It was obvious that this growth was

involving the whole thickness of the rectal wall and that it extended into the perirectal tissues. A transverse colostomy was performed to the left of the midline above the umbilicus. The proximal and distal limbs of the colon were sutured together. The distal colon and rectum were then washed out daily from both the distal stump of the colostomy and from the rectum. This procedure was carried out for one month. At the end of that time the abdomen was reopened, and the pelvic colon and the upper third of the rectum were excised, with anastomosis of the mobilized iliac colon to the rectal stump, by means of a tube sutured into the proximal loop and passed down into the rectum and through the anus. The patient made an uninterrupted recovery after this operation. (Specimen shown in fig. 2 and fig. 3.)

*Pathologist's report* [Dr. Cuthbert Dukes] :

Gross characters : The specimen consisted of a segment of the bowel from the region of the recto-sigmoidal junction measuring 6 in. in length removed by tube resection. An ulcerating and constricting growth 1½ in. in diameter completely encircled the distal end of



FIG. 2.—Carcinoma of recto-sigmoid junction removed by conservative excision.

the specimen, there being 1 in. free margin here and 3½ in. at the proximal end. There was gross evidence of extrarectal spread. A dissection was made of the extramural lymphatics and nine glands were removed for section.

Microscopic structure : The tumour is an adenocarcinoma. Histological malignancy Grade 1.

Methods of spread : (1) By direct continuity : the tumour had spread extensively by direct continuity into the perirectal fat. (2) Vascular spread : The main branch of the haemorrhoidal vein was found to be thrombosed and its walls infiltrated with carcinoma cells. (3) Lymphatic spread : Metastases were present in six of the regional and haemorrhoidal glands. (9 glands examined, fig. 3.)

Classification : Carcinoma of rectum with extensive vascular and lymphatic spread [C2 Case].

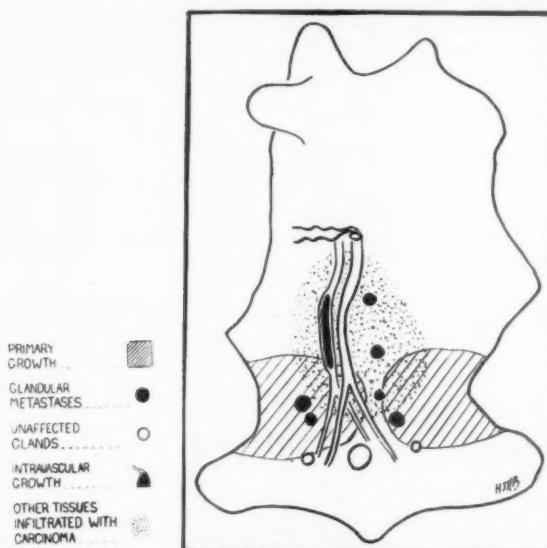


FIG. 3.—Diagrammatic representation of dissection of specimen (fig. 2) to show extent of spread.

Nine weeks after excision, a sigmoidoscope was passed through the anastomotic line and granulation tissue could be seen at the line of suture. A piece of this tissue was removed and proved to be adenocarcinoma. In view of this, the patient was advised to have a radical excision of the rectum. Five months after the original conservative excision, abdomino-perineal excision of the rectum was performed, leaving a left inguinal colostomy. This operation was extremely difficult owing to peri-rectal inflammation following the previous excision. The patient again made an uninterrupted recovery, and two months after this operation the transverse colostomy was closed.

The patient, however, gradually went downhill, and died five months after the abdomino-perineal excision. Post-mortem examination revealed local recurrence in the pelvis.

This case illustrates the futility of performing conservative resection in an unsuitable case. The growth had involved the whole thickness of the rectal wall and had spread to the peri-rectal tissues and, further, there were glandular metastases and thrombosis of a haemorrhoidal vein.

*Pathologist's report [Dr. Cuthbert Dukes]:*

**Gross characters:** The specimen (fig. 4) consisted of the remains of the rectum and pelvic colon and measured 10 in. in length. Five inches above the ano-rectal line the lumen of the bowel was much constricted and the wall of the rectum was infiltrated with hard tissue. There was no definite ulceration or tumour apart from this, but a white linear scar was situated 2 in. below the constriction.

**Microscopic structure:** In the region of the scar the rectal wall is infiltrated with adenocarcinoma. Histological malignancy Grade 1. Sections through the region from which a malignant adenoma was removed do not show any sign of recurrence.

**Methods of spread:** (1) By direct continuity: The tumour had spread extensively into the peri-rectal fat. (2) Vascular spread: One of the branches of the haemorrhoidal vein



FIG. 4.—Recurrent carcinoma removed by abdomino-perineal excision.

was completely embedded in a carcinomatous deposit arising probably from perivascular permeation. (8) Lymphatic spread : Large metastases were present in three of the six regional and haemorrhoidal glands.

Classification : Carcinoma of the rectum, with extensive lymphatic and vascular spread [C2 Case].

**Diverticulitis of the Sigmoid Colon with Vesico-colic Fistula, treated by Colectomy.—C. NAUNTON MORGAN, F.R.C.S.**

J. M., male, aged 63.

*History.*—Complained of increased frequency of micturition, and increased constipation for three months. No diarrhoea or attacks of abdominal distension. Had lost 3 st. in weight in seven months.

*On examination.*—Rectal examination and sigmoidoscopy revealed nothing abnormal. Barium-enema examination showed a localized area of diverticulitis at the apex of a loop of sigmoid colon. The urine was heavily infected with *Bacillus coli* and cystoscopy showed a generalized cystitis with puckering and oedema of the left side of the bladder near the fundus. No bubbles of air were seen coming from this puckered area.

*Operation.*—On January 13, 1938, the abdomen was opened and a loop of sigmoid colon was found firmly adherent to the fundus of the bladder. An attempt was made to separate the colon from the bladder, but it was soon realized that a colic fistula was present. A portion of the bladder—about the size of half a crown—was therefore removed and the colon was mobilized. The bladder was repaired on its peritoneal

surface and extraperitoneal suprapubic drainage was also carried out. A small incision was made in the left iliac fossa and the mobilized colon and attached bladder were extraperitonealized and excised by Paul's method. Within a month of the operation the patient's bladder had completely healed and he was passing urine normally. An enterotome was inserted into the colostomy on the ninth day, and when it was removed the patient began to pass faeces *per rectum*.

*Comment.*—It must be very unusual to be able to excise a part of the colon and a portion of the bladder in the case of a vesico-colic fistula. This case, however, seemed to be ideal for radical treatment of the fistula, owing to the extremely localized area of diverticulitis and the long thin sigmoid loop, without evidence of obstruction.

The specimen consists of several inches of the sigmoid colon and an area of bladder the size of half a crown, with a fistulous opening passing from a diverticulum into the bladder.

JOINT DISCUSSION No. 8

**Section of Physical Medicine and Section of Dermatology**

Chairman—F. D. HOWITT, C.V.O., M.D. (President of the Section of Physical Medicine)

[January 21, 1938]

**DISCUSSION ON THE SKIN MANIFESTATIONS IN RHEUMATISM**

**Dr. H. W. Barber:** It is, I think, very fitting that our two Sections should hold this joint discussion, because those who practise what are called physical methods in the treatment of various chronic diseases, and those whose interest lies chiefly in the protean manifestations of what we vaguely term rheumatism, have realized more than most the great importance of the proper functioning of the skin. This was brought out very clearly at the Conference on Rheumatic Diseases held at Bath in 1928, when one speaker after another emphasized the disturbances of the cutaneous circulation and of sweat-secretion that obtain in the rheumatic and pre-rheumatic states.

To quote Llewellyn [1]

"The primary signs of physiological inadequacy in rheumatic subjects are instability of the skin's blood supply and sweat secretion. This supplies us with what should be a basal principle in prophylaxis, namely the maintenance of the skin's functional efficiency, the importance of which has been gravely underestimated. For though the skin is a 'living' vesture, yet seemingly in rheumatism we hold it less than raiment. Otherwise, why so much of the hygiene of clothing, so little of skin hygiene?"

These words were spoken nearly ten years ago; their significance is now widely recognized, and I think physiotherapists will agree that stimulation of the skin by one method or another is one of their chief aims. But, although the methods have changed, the idea is, of course, a very old one, since for centuries past stimulation of the skin by blistering and other means has been a recognized form of treatment for many diseases.

This leads us to an aspect of the subject which is more germane to the present discussion, namely the association—and more particularly the alternation—of certain skin eruptions, with symptoms referable to other organs and structures. The so-called allergic person provides, perhaps, the best example of this; thus when his eczema is at its worst, he is usually free from asthma or migraine, and vice versa, and I have met several psoriatics who refuse treatment for their eruption because its disappearance leaves them crippled with rheumatism. All medical students at the beginning of their clinical studies should read the writings of that great clinician, Louis Brocq [2], on this subject. In the famous chapter in his "Cliniques Dermatologiques" entitled "Les Fluxions et les Alternances Morbides" he describes with meticulous accuracy the medical life-history of one Jean X—(who was Brocq himself), together with those of 19 of his relatives. Brocq was subject throughout his strenuous and courageous life to most of the non-specific diseases that affect

mankind, and these alternated in striking fashion, but whenever he suffered from one of his various skin eruptions—urticaria, carbuncles and boils, eczema, prurigo, and the psoriasisiform type of seborrhoeic dermatitis—he was free from his other symptoms which, to name only a few, included asthma, paroxysmal rhinitis, migraine, gastro-intestinal upsets, rheumatism, and neuralgia. It is of interest that all his crises of this or that symptom could be brought to an end and their recurrence prevented by a strict dietetic régime, only to return when he relaxed it.

It is the problem of the non-specific diseases which concerns us to-day, and for non-specific diseases there are no specific treatments. It is absurd to talk of a "cure" for asthma, or eczema, or rheumatism. It is a question of what will cure Mr. A.'s asthma or Mrs. B.'s eczema, and it is for the clinician to decide what are the likely causative factors in each individual case, calling upon the laboratory worker, when necessary, to substantiate his conclusions. To be able to do this, however, the clinician must try to avoid falling into the trap that has at times ensnared most of us, namely, to regard the non-specific diseases from one angle, be it bacteriological, biochemical, or psychological, and therefore to attempt to treat every case accordingly by the same method. If one looks back over the history of the non-specific diseases in recent years, one finds that it records the rise and fall of one new idea or method of treatment after another—focal infection, vaccine therapy, intestinal stasis and toxæmia, cutaneous tests for sensitiveness to foods or other allergens, ultra-violet light radiation, shock-therapy, and so on: each of these seemed so full of promise, each to a varying extent has fallen from grace. Yet there is virtue in all of them.

The crux of the matter in a nutshell is this, that the treatment of the sufferer from a specific disease, such as syphilis, malaria, or diphtheria, is with certain reservations cut and dried, whereas every patient with some non-specific (or apparently non-specific) disease presents a separate problem, since the same symptoms may be provoked in different cases by factors which at first sight have nothing whatever in common. It is for this reason that I have submitted a brief summary of what I believe to be the chief factors which may predispose to, or influence, the development of many non-specific diseases.

#### *Factors Operative in the Aëtiology of Non-specific Diseases*

- (1) Hereditary and familial predisposition.
- (2) Inborn or acquired dysfunction of the endocrine-autonomic system.
- (3) Environment and mode of life.
- (4) Diet.
- (5) Infections, acute or chronic.
- (6) Psychological disturbances, or nerve-strain.
- (7) Inborn, or acquired, errors of metabolism.

(1) The influence of hereditary and familial predisposition is observed in the allergic syndrome of symptoms, in rheumatoid arthritis, in gout, in psoriasis, and in disturbances of the endocrine-autonomic system, e.g. Graves' disease, vitiligo, and alopecia areata.

(2) An inborn dysfunction or lack of balance of the endocrine-autonomic system is evident in allergic subjects and in some cases of Graves' disease. An acquired upset of the endocrine-autonomic balance may result from environment and climate, from a faulty diet, from infections, acute and chronic, and from psychological disturbances.

(3) Environment is an important factor in the allergic syndrome of symptoms as regards exposure to potential antigens, psychological disturbances, and climatic condition; also in certain forms of rheumatism. Climatic influences exert their effect by their action on the thyroid-adrenal-sympathetic apparatus, and by predisposing to certain infections. Mode of life is of obvious importance as regards exercise, exposure of the skin to sunlight and air, &c., in metabolic errors, the allergic syndrome, and disturbances of the endocrine-autonomic system.

(4) Diet. Undernutrition, resulting from insufficient or improper food and deficiency of vitamins and mineral salts, is frequently a basic factor of paramount importance,

predisposing to acute and chronic infections and to disorders of the digestive, haemopoietic, endocrine, and nervous systems. Overnutrition and excess of alcohol have an obvious influence upon metabolic diseases. Specific food-sensitivity may be a factor, particularly in allergic subjects.

(5) Acute and chronic infections are, directly or indirectly, responsible for a great variety of non-specific diseases. They may provoke various types of inflammatory reaction in the different organs and tissues (direct action), and from their effect upon the endocrine-autonomic system (particularly on the thyroid-adrenal apparatus) may give rise to disorders dependent upon a dysfunction of this system (indirect action). The direct and indirect effects of infection may occur together in the same person.

(6) The importance of psychological disturbances and prolonged nervous tension cannot in these days be overestimated. They may be, even in young children, the chief factors in provoking the so-called allergic syndrome of symptoms (asthma, paroxysmal rhinorrhœa, migraine, urticaria, angeioneurotic œdema, eczema, pruritus, prurigo, and gastro-intestinal disturbances). They, admittedly, often play a part in the aetiology of rheumatoid arthritis, hyperpiesis, hyperthyroidism, and Graves' disease; and of vitiligo and alopecia areata. Like acute and chronic infections, they exert their effect upon the endocrine-autonomic system.

(7) Errors of metabolism are extremely common even in those in apparently good health; for example, disturbances of the acid-base equilibrium, minor degrees of hepatic insufficiency, and retention of fluid. Many morbid conditions—e.g. the allergic syndrome, gout, hyperpiesis, and pernicious anaemia—are associated with fluid-retention. During the active stage of symptoms in allergic disorders and gout there is oliguria, increased urinary concentration and acidity, and deposition of urates, which, as the symptoms subside, are succeeded by diuresis and decreased urinary concentration and acidity. A shift of the acid-base equilibrium to the acid side is followed by retention of water and mineral salts, while a shift to the alkaline side is followed by increased water and mineral elimination.

I come now to the consideration of certain conditions of the skin likely to be associated with the various forms of rheumatism, including gout. These I have tentatively classified into three groups.

*Certain Conditions of the Skin Likely to be Associated with the Various Forms of Rheumatism, including Gout*

We have to consider:—

(A) Banal eruptions, or symptoms referable to the skin, which may, and often do, occur in association with rheumatic disorders, such as fibrositis, fibromyositis, and gout, or alternate with them: as examples, urticaria, eczema, pruritus, and prurigo, may be cited.

(B) Eruptions which are, or have been, thought to be closely associated with definite forms of rheumatic disease, viz.:—

*In association with rheumatic fever.*

Erythema multiforme.

Erythema annulare rheumaticum (Lehndorff and Leiner: Abt.).

Erythema scarlatiniforme.

The cutaneous and subcutaneous forms of rheumatic nodule.

Erythema nodosum.

Purpura (peliosis rheumatica).

*In association with gonococcal arthritis.*

Keratoderma blenorragica.

*In association with rheumatoid arthritis.*

Psoriasis.

Lupus erythematosus.

Subcutaneous nodules.

*In association with chronic fibromyositic and articular rheumatism of middle age.*

Erythema induratum (non-tuberculous type: "nodosité rheumatismale").

*In association with gout.*

Palmar and plantar hyperkeratosis.

To this group may be added a widespread form of granuloma annulare, associated with chronic rheumatism of the fibromyositic type, both conditions apparently depending upon a chronic streptococcal infection.

(C) Cutaneous changes, presumably associated with disturbances of the endocrine-autonomic system, which occur with some frequency in association with rheumatoid arthritis.

- Acro-asphyxia with or without Raynaud's disease.
- Disturbances of sweat secretion—hyperhidrosis and anhidrosis.
- Cutaneous atrophy, approaching the "glossy skin" of Paget.
- Pruritus and prurigo.
- Hyperpigmentation and vitiligo.
- Scleroderma.
- Alopecia areata.

With regard to Group A I do not propose to say very much. It includes the commoner reactions of the skin (eczema and urticaria) which often are associated, or alternate, with symptoms referable to other organs, e.g. asthma, paroxysmal rhinorrhœa, migraine, articular gout, and rheumatism affecting the muscles, fibrous tissues, or joints. In some cases the cause of the alternative symptoms is the same; for example, a focal infection may be responsible both for an eczema—or urticaria—and for rheumatism occurring in the same patient; in others one symptom may be provoked by one cause, and a different one by another. There is a factor in many of these cases, which has not in this country received the recognition it deserves, namely retention of fluid. The importance and significance of this have been fully discussed by Eugene Földes [3].

Whatever the primary provoking factor may be, the development of many of these symptoms—eczema, urticaria, migraine, gout—is accompanied by retention of fluid, and it is the site at which the retained fluid is mobilized that determines the nature of the symptom—in eczema in the epidermis, in urticaria in the dermis, in angioneurotic oedema in the subcutaneous tissue, in migraine in the brain, in paroxysmal hydrarthrosis in the joint-structures, and so on. From a practical standpoint, apart from determining, when possible, the primary provoking causes, the recurrence of these symptoms can often be prevented by a diet and other measures designed to inhibit retention of fluid, and to favour its elimination.

Group B comprises eruptions which are, or have been, thought to be closely associated with definite forms of rheumatic disease. As the interests of the Section of Physical Medicine are hardly concerned with rheumatic fever, I shall say little about the eruptions that have been thought to be associated with it. It is doubtful whether the connexion between erythema multiforme, erythema nodosum, and acute rheumatism is as close as has been thought in the past. Both types of eruption may be provoked, and in some cases doubtless caused, by streptococcal infection of the throat; and pain and swelling of the joints may occur with them. In rheumatic fever the haemolytic streptococcus also plays an important part, although there is some evidence that a filtrable virus is the primary invader. But it is rare to see either erythema multiforme or erythema nodosum during attacks of true rheumatic fever with endocarditis, although it is possible, as I have suggested elsewhere [4], that the cutaneous eruption renders involvement of the heart and other structures less likely.

Moreover, it has now been established that in the majority of cases, erythema nodosum is a manifestation of a recent tuberculous infection. With regard to erythema multiforme of the classical Hebra type, although the association with streptococcal infection, either in the throat or elsewhere, is common, I have been impressed of late by its frequent association with herpes simplex, to which Forman and Whitwell have drawn attention [5]. Some of my own recurrent cases have suggested that it might sometimes represent a generalized cutaneous reaction to the herpes virus.

Coming now to the eruptions which may be associated with rheumatoid arthritis, the most important is psoriasis. Of course psoriasis is so common a disease that its

fortuitous occurrence with arthritis and other rheumatic disorders might be expected. Nevertheless most of us are probably agreed that the association is too frequent to be a coincidence, and in psoriasis arthropathica we have a well-defined syndrome. Dr. Hunt, who follows me, is going to confine her remarks to psoriasis, so that I shall deal only with a few points. The first is whether psoriasis is due to infection with an unknown specific organism—possibly, as has been suggested by Desaux and Prétet [6], a filtrable virus—or whether, like eczema, urticaria, and the erythema, it is a non-specific reaction of the skin. The factors which provoke an outbreak of psoriasis undoubtedly differ widely in different cases, but this is not conclusive evidence as to its non-specific nature, since the same is true of herpes simplex. For the present, however, it may be included in the group of non-specific eruptions.

I have set out in the summary on page 32 what I think are the chief points in the aetiology of the disease, and I need not reiterate them, but I should like to dilate a little further on the parallel that may be drawn between psoriasis and rheumatism. I think we can, on the one hand, compare the psoriasis of childhood with rheumatic fever, and on the other, the psoriasis of adult life with the adult manifestations of the rheumatic state. In my own experience, when psoriasis appears for the first time in childhood, there is nearly always an evident association with streptococcal infection in the throat. It often breaks out like an acute exanthem shortly after an attack of tonsillitis or of scarlet fever, and widespread exacerbations occur with subsequent attacks of tonsillitis. The eruption often, of course, persists into adult life, and in such cases one usually finds a chronic infection of the throat with the haemolytic streptococcus. In this group of cases, whether in children or adults, effective treatment of the throat infection—and this, I may say, does not consist only of enucleating infected tonsils—has appeared to be curative in many instances.

When, however, psoriasis appears for the first time in adult life, the same multiplicity of provoking factors that prevails in the rheumatism of adults is observed. I am satisfied that there is one group of cases in which focal streptococcal infection from the teeth, nasal sinuses, or elsewhere, is all-important, just as it may be in rheumatism. In other cases infection with, or toxæmia from, other organisms, such as *B. coli* or coliform variants may, perhaps, be a factor. In many, however, the evidence of any infection seems to be entirely lacking, but metabolic errors are present, the treatment of which may cause the eruption to disappear. Finally, it must be admitted that in some psoriatics the most exhaustive investigation fails to provide any clue either to the causation or the treatment of their disease. In some of these the nervous or psychological factor is apparent, but exactly how it exerts its influence is a mystery.

With regard to the syndrome arthropathic psoriasis, I would emphasize the peculiar tendency to involvement and deformity of the terminal interphalangeal joints of the fingers and toes, together with the severe psoriatic changes in the corresponding nails. I shall publish elsewhere in detail a case of this disease—which has been under my observation for ten years—in which without any doubt severe focal infection in numerous dead teeth was responsible for both the psoriasis and the arthritis. Apart from some deformity in a few interphalangeal joints, the patient is now well. In some other cases of psoriasis arthropathica, however, I have not been able to establish that an infection was the cause of the disease.

By a curious coincidence I saw a case in consultation only a few days ago, which is of great interest in this connexion, as it would seem to indicate that the clinical picture of psoriasis arthropathica can be produced—or at least imitated—by gout.

The patient was a woman, aged 61, who in 1934 had her first attack of acute articular gout in the first metatarsophalangeal joints. Later similar attacks occurred in the ankles, knees, and some of the finger-joints. In August last year psoriasis

first appeared around the terminal interphalangeal joint of the left middle finger, which was already deformed by gout. It subsequently spread to other parts and is now extensive. All the finger-nails, and some of the toe-nails, exhibit typical psoriatic changes, but that of the left middle finger is most severely involved, so that, with the swelling and deformity of the adjacent interphalangeal joint, exactly the same feature is present that I have emphasized as being so characteristic of arthopathic psoriasis. Apart from the marked changes in this joint and some varying degree of swelling in the knee-joints, there is little deformity in the other articulations. Radiograms of the joints are to be taken and the blood uric acid estimated, but there is no doubt that the case is one of true arthritic gout, associated with psoriasis, and reproducing the clinical picture of psoriasis arthropathica. (N.B.—The blood uric acid was 10.3 mgm. per 100 c.c.)

Here, then, we have two patients, of whom the first was undoubtedly a classical example of psoriasis arthropathica, with joint-changes typical of rheumatoid arthritis, except for the severe involvement of the terminal interphalangeal joints; and the second, an equally typical case of arthritic gout with psoriasis, in whom the same nail-joint syndrome, as one might term it, is present. In the first case, as I have said, focal streptococcal infection from the teeth was unquestionably the *fons et origo malorum*; in the second, there is no evidence of any focal infection, and the causative factor is a metabolic one.

#### *Summary of Factors in the Aetiology of Psoriasis*

As with rheumatic disorders, all the factors cited above as operative in the aetiology of non-specific diseases must be considered in psoriasis, and for the present it may be regarded as a non-specific cutaneous reaction (cp. eczema, urticaria, and the erythema), the tendency to which is hereditary and familial in about 30% of cases. Familial association with rheumatism or rheumatoid arthritis is common (80% according to Hunt). The eruption may occur or alternate with ("alternances morbides" of Brocq) various types of rheumatism—fibromyositis, rheumatoid arthritis, osteo-arthritis, and gout. As regards provoking factors, apart from heredity, the following may be considered:—

(a) *Environment*.—In winter (as a rule) and in cold countries psoriasis is more prevalent than in summer and warm climates. In the tropics it is rare (Kayser)—cp. rheumatism.

(b) *Diet and errors of metabolism*.—No constant effects are apparently produced by various dietetic régimes. Schamberg, as a result of experimental studies, advised a low-protein diet, excluding animal protein, and in some cases the effect is striking. Other cases, however, respond to a low carbohydrate-fat dietary. Grütz [7] employing Bürger's test, asserted that there is a disturbance of fat-metabolism in psoriatics, and prescribes an almost fat-free diet. The good results he obtained from this treatment have not, except in some cases, been observed in this country. Some psoriatics, in whom the blood uric acid is high, respond remarkably to the dietetic and internal treatment employed in gout. Excess of alcohol aggravates psoriasis, and in confirmed alcoholics no treatment is effective unless complete abstention is enforced.

(c) *Infections, acute and chronic*.—As with some other dermatoses (e.g. eczema, prurigo), certain acute infections, such as pneumonia, typhoid, and some of the exanthemata, usually cause an existing psoriasis temporarily to disappear. Streptococcal infections, however, almost invariably provoke an acute exacerbation of the eruption. The influence of streptococcal infection upon psoriasis in many cases is one of the most striking clinical features of the disease. The chief points concerning this relationship are as follows:—

(i) The eruption often breaks out acutely like an exanthem after tonsillitis and scarlet fever. Fresh exacerbations follow subsequent attacks of tonsillitis.

(ii) When psoriasis appears for the first time in childhood or adolescence, there is in the majority of cases an association with acute or chronic streptococcal infection of the throat. In these cases successful treatment of the infection, in childhood or adult life, may be apparently curative.

(iii) There is a group of cases of psoriasis appearing first in adult life, in which focal infection in the teeth, nasal sinuses, or elsewhere, seems to be the provoking factor.

(iv) Streptococcal septicæmia has a remarkable effect upon an existing psoriasis. The eruption spreads rapidly, and serous oozing and visible pustule-formation occur in the patches. Eventually a generalized exfoliative dermatitis may develop. These cases are not necessarily fatal.

(v) In some psoriatics a focal streptococcal infection, usually in the tonsils, may provoke a pustular form of the eruption, particularly on the palms and soles. The condition is comparable clinically and aetiologically to the so-called "pustular bacteride" occurring in non-psoriatics. In both conditions the pustules are sterile.

A comparison may be made between the influence of streptococcal infection upon psoriasis and its rôle in rheumatism. In rheumatic fever and in the psoriasis of childhood, streptococcal infection of the throat, whatever may be its exact significance, plays a very important part. The two diseases may develop after a "silent" period of about one to three weeks following either tonsillitis or scarlet fever, and in both subsequent attacks of tonsillitis are followed by recrudescences even in adults. In rheumatoid arthritis and in psoriasis beginning in adult life, focal infection in the teeth, nasal sinuses, or elsewhere, may be the chief provoking factor.

*On the other hand, in many adult cases of psoriasis there is no evidence that streptococcal infection plays any part whatever*, and the same is true of some cases of rheumatoid arthritis. It is likely, however, that infection with other organisms, e.g. *B. coli* and *coli*-variants, may in some cases be a factor in both diseases. Certainly psoriasis may be influenced by *B. coli* infection of the urinary tract.

*Psoriasis arthropathica*.—Apart from the association of psoriasis with various forms of rheumatic disease and gout, there is a syndrome—arthropathic psoriasis—which possesses certain distinctive features. The arthritis resembles clinically and roentgenographically atrophic arthritis, and the deformities may be very severe. One feature, however, is peculiar, namely the tendency to involvement of the *terminal* interphalangeal joints of the fingers and toes, which is rare except in severe and late cases of non-psoriatic arthritis, and the severe psoriatic changes in the nails adjacent to the affected joints. Moreover, intermittent hydrarthrosis of the larger joints is commoner than in non-psoriatic arthritis. In some cases focal streptococcal infection appears to be the chief aetiological factor, as in the case observed in which infection from numerous dead teeth was unquestionably responsible for both the psoriasis and the arthritis, but in other cases this is not apparent.

(d) *The psychological factor*.—Bunnemann has described a case in which psoriasis appeared to represent a symbolic neurosis, and acute outbreaks after shock or strain are not uncommon. In one severe case observed, nerve-strain was the only factor which appeared to provoke the exacerbations.

*Erythema induratum*.—An important, although rather uncommon, eruption, which is closely associated with chronic rheumatism in middle age, is the non-tuberculous form of erythema induratum. It was carefully described by Whitfield [8] in 1908. It consists of reddish or bluish-red subcutaneous nodules of varying size and contour, the majority being circular, but some forming flat indurated plaques. As in the tuberculous form of erythema induratum—often termed Bazin's disease—the lesions occur for the most part on the lower portions of the legs and in persons with acro-asphyxia, but they are also found on other parts, for example around the knees, on the arms, and in one of Whitfield's cases, on the ears. They are extremely painful, much more so than those of Bazin's disease. They subside quickly if the patient rests in bed, but fresh crops continue to appear when she is up. In Whitfield's experience, the condition occurs "exclusively in women of from 35 to 45 years of age", but I have described [9] a typical case in a middle-aged man, in whom the extraction of several infected dead teeth was rapidly and permanently curative.

In both types of erythema induratum the inflammatory reaction involves the walls of the small subcutaneous veins, whereas in erythema nodosum, as Hadfield [10] has shown, there is an acute and widespread arteriolitis in the subcutaneous fat. In both conditions there is fat necrosis.

Whitfield has emphasized the association of this non-tuberculous form of erythema induratum with chronic rheumatism, and I agree with him that it is "the result of septic absorption, often from the teeth". In other words, it may be regarded as

one form of subcutaneous streptococcide. It is of interest that there is thus a tuberculous and a streptococcal form of both erythema nodosum and erythema induratum. The difference between the two eruptions is that in the first the inflammatory reaction is in connexion with an arteriole, in the latter with a small vein.

I should have liked to say something about the conditions I have included in Group C, namely the cutaneous changes associated with disturbances of the endocrine-autonomic system, and in particular about the widespread form of circumscribed scleroderma or morphoea, of which I have had a few most interesting cases illustrating its association with rheumatoid arthritis. But I shall conclude with a brief reference to a condition which I believe to be a manifestation of true gout. It is one form of keratoderma of the palms and soles. My attention was drawn to this several years ago, and I have been able to collect a number of cases. It occurs in both sexes and is characterized by :—

(1) *An erythema* of the palmar and plantar surfaces, extending on to the lateral surfaces of the hands and feet.

(2) *Hyperkeratosis*, occurring chiefly at sites of pressure and often associated with painful fissures due to splitting of the hypertrophied horny layer.

(3) *Subjective symptoms* of itching and burning.

Most of my patients have been of middle or late-middle age, and of the plethoric "gouty" type, but I have seen it in early adult life and in old persons. Hyperacidity of the urine, with deposits of urates or of uric acid, is found, and the blood uric acid is high, even in the younger patients. The condition may improve in striking fashion under anti-gout therapy.

It must not be confused, however, with the keratoderma climacterium of Haxthausen [11], which is met with exclusively in women at the climacteric, and may be associated with the post-climacteric triad of Gram—obesity, arterial hypertension, and arthritis. In one of my cases, Dr. P. M. F. Bishop succeeded in causing the condition to disappear, with adequate doses of ovarian follicular hormone. It relapsed when this was discontinued, but disappeared again when treatment was resumed.

#### REFERENCES

- 1 LLEWELLYN, R. L. J., *Proc. Conf. Rheum. Dis.*, 1928, Bath, 111.
- 2 BROcq, L., "Cliniques dermatologiques", Paris, 1924, 47.
- 3 FÖLDÉS, E., "A new approach to dietetic therapy", Boston, 1938.
- 4 BARBER, H. W., "Lettsomian lectures", *Lancet*, 1929 (ii), 483.
- 5 FORMAN, L., and WHITWELL, G. P. B., *Brit. J. Dermat.*, 1934, **46**, 909.
- 6 DESAUX, A., and PRÉTET, A., *Delibérat. Cong. Derm. Int.*, Budapest, 1936, **2**, 683.
- 7 GRÜTZ, O., *Deutsche med. Wochenschr.*, 1934, **60**, 1039.
- 8 WHITFIELD, A., *Brit. J. Dermat.*, 1909, **21**, 1.
- 9 BARBER, H. W., "Lettsomian lectures", *Lancet*, 1929 (ii), 483.
- 10 HADFIELD, G., "Erythema nodosum", *J. Odery Symes*, Bristol, 1928, 18.
- 11 HAXTHAUSEN, H., *Brit. J. Dermat.*, 1934, **46**, 161.

**Dr. Elizabeth Hunt : Psoriasis and rheumatism.**—It has long been recognized that psoriasis is often associated with rheumatism of various forms, occurring either in the same individual or in a near relative, but no detailed records exist of the frequency of the incidence of this association.

In 1933 the *Lancet* [1] published a brief communication from me on a small series of 53 cases of psoriasis in which the family histories and the patients' histories, in regard to rheumatic manifestations, such as rheumatism, rheumatic heart, chorea, arthritis, tonsillitis, and quinsy, had been investigated.

A family history of rheumatic manifestations was obtained in a much higher percentage of the cases than a family history of psoriasis, though it is commonly taught that psoriasis is a familial disease.

Including a further 22 cases, with the 53 cases of psoriasis originally reported, making a total of 75 : 52 cases gave a family history of rheumatic manifestations, viz. 70% ; 23 cases gave a family history of psoriasis, viz. 30%.

The occurrence of rheumatic manifestations in the individual histories of psoriasis patients is well illustrated in the following table, in which a few case histories of patients with mitral stenosis are set out in parallel columns with a similar number of typical case histories of psoriasis patients whose family histories are also shown.

No.	Age	Mitral stenosis	No.	Age	Psoriasis	Family history
I	37	(1) Rheumatic fever (aged 15); (2) Rheumatic fever (after parturition)	I	62	Rheumatic fever (aged 16) Psoriasis in convalescence	Rheumatism
II	32	Rheumatic fever (aged 9) Chorea (aged 10)	II	40	Rheumatic fever (aged 7) Psoriasis in convalescence Sore throats	Psoriasis Rheumatoid arthritis and psoriasis
III	43	Rheumatic fever (aged 25) after parturition	III	56	Psoriasis (aged 21) after parturition	Tonsillitis Arthritis Psoriasis
IV	33	Sore throats Rheumatic pains Chorea in pregnancy	IV	38	Rheumatic pains Psoriasis (aged 35) in pregnancy	Rheumatism Tonsillitis
V	34	Acute rheumatism (aged 26)	V	47	Acute rheumatism (aged 25) Psoriasis (aged 27)	Not obtained
VI	33	Growing pains Sore throats	VI	23	Growing pains Sore throats	Rheumatic fever Rheumatism
VII	33	Rheumatic pains	VII	32	Sore throats Rheumatic pains	Mitral stenosis Rheumatoid arthritis
VIII	30	Sore throats Rheumatism	VIII	55	Tonsillitis Rheumatism	Chorea Rheumatic heart
IX	29	Scarlet fever (aged 8) Rheumatism	IX	44	Scarlet fever (aged 10) Rheumatism Quinsy	Rheumatic fever Rheumatic heart

The extraordinary similarity of the case histories preceding these two different and seemingly unrelated conditions is at once apparent from this table, and it is obvious that we cannot accept such histories as constituting the aetiological factors when they precede one condition, valvular heart affection, and completely ignore them when they precede a second condition, a comparatively benign skin affection, psoriasis.

It is probable that the benign character of psoriasis has diverted attention from its relationship to rheumatic infection, and the fact that, though psoriasis is frequently found in association with rheumatic manifestations and the various forms of arthritis, it is not observed with those grave manifestations of rheumatic infection, chorea, and rheumatic heart disease.

Comparing all the cases of psoriasis and of mitral stenosis in my two series, it was found that 50% of the mitral stenosis cases gave a history of chorea. In no case is chorea recorded in the psoriasis cases. The cardiac cases reported recurrent attacks of rheumatic fever. I have not found, so far, amongst psoriasis cases a history of a recurrent attack of rheumatic fever following the evolution of psoriasis. Lastly, psoriasis patients do not appear to develop mitral stenosis. For some years I have been searching for a psoriasis patient suffering from a rheumatic heart, but have failed so far in my search.

When we consider the histories of psoriasis patients, their environment, and their family predisposition to rheumatic affections as shown in the figures and table above, the immunity of the psoriasis members of rheumatic families to the graver

complications of rheumatic infection appears more significant, and invites a closer comparative study.

An analogy may be drawn between the histopathology of the lesion of psoriasis and of the rheumatic nodule [2]. Both lesions evolve in a similar manner, and in both the cells in the neighbourhood of the lesions proliferate, the ultimate difference in the two lesions being attributable to differences in the types of the cells involved. Both lesions also may proceed to abscess formation, which in the case of the experimental rheumatic nodule has been shown to occur in a sensitized animal with smaller doses of streptococcal than in a normal or immune animal, indicating that allergy plays a part [3].

Definite proof of such an allergic reaction in the case of the psoriasis lesion is lacking, but the eruption presents many features peculiar to allergic conditions, such as a family predisposition, seasonal recurrences, spontaneous remissions, and a frequent association with an infective focus.

To these may be added the symptoms of a psoriasis eruption which are peculiar to the tissue—the epidermis—in which the lesions occur. After the manner of a holocrine (Ranvier) gland the epidermis is continually producing a secretion of horny scales formed by the complete disintegration of its cells. In psoriasis there is an excessive secretion of these horny scales.

Excessive secretion from sensitized tissue is frequently observed in allergic conditions, such as e.g. hay fever, the character of the secretion varying with the type of the tissue affected. The tissues affected by the antigens of rheumatic infection are the poorly vascularized tissues such as the pericardium, the mitral valve, synovial membrane, and the sheaths of muscles, &c. The epidermis which is lacking in blood-vessels may be included in this category.

Sensitization of cells of the epidermis by a blood-borne antigen has been conclusively demonstrated by Naegeli, de Quervain, and Stalder [4] in a case of antipyrrin idiosyncrasy, and they proved experimentally that only certain cells, viz. the cells of the rete malpighii, were affected in their case.

The eruption of psoriasis presents features in common with this example of epidermal sensitization by an endogenous route. In both an erythema is the initial sign, and in both dilatation of the papillary vessels occurs, a sign which has long been regarded as pathognomonic of the psoriasis lesion. Both lesions also are confined to the epidermis, and on histological and on clinical grounds it may be claimed that the chain of symptoms known as psoriasis could result from sensitization of the cells of the basal layer of the epidermis.

The interaction of antigen with antibody provokes a reaction of the cells in which the antibodies are fixed. In the case of the psoriasis lesion the increased proliferation of the cells in the neighbourhood of the lesion points to a reaction of the cells of the basal layer of the epidermis, the only cells which are reproductive, and the manifestations of psoriasis are explicable as a disturbance of the normal function of these cells in consequence of this. If the normal rate of reproduction of basal cells is speeded up, the progress of these cells towards the surface becomes so rapid that the changes they should normally undergo in their progress outwards cannot be completed, and they reach the surface in an immature state, imperfectly keratinized. An excessive secretion of scales results, the chemical composition of which differs from the normal, two of the characteristic signs of psoriasis. Variations in the speed of proliferation of the basal cells would give rise to those differences in the amount of scaling produced, with which we are familiar in cases of psoriasis.

It is recognized that in many allergic conditions the same symptoms can be produced by a variety of antigens, and if, as is here suggested, a psoriasis eruption results from hyperactivity of the basal layer of the epidermis due to sensitization, it may be inferred that the antigens which provoke such a reaction need not always be the same. This would explain many of the clinical findings in psoriasis, such

as the association of psoriasis with streptococcal infections; the association with infective conditions of the antrum, the mastoid or with oral sepsis, the recurrent cases of psoriasis and hydrarthrosis; and the association of psoriasis with arthritis of various forms. In this connexion also, Zeidler's [5] observations on cases of psoriasis and hay fever in which the psoriasis lesions receded with the hay fever symptoms, and his findings that many psoriasis patients who had not hay fever, are sensitized to pollens, are of interest, especially when patients report a seasonal recurrence of the eruption in summer.

In relation to the rheumatic infections, two features of the clinical manifestations of psoriasis are of special interest. In the first place a latent period of some weeks occurs between the time of the initial infection and the onset of the eruption, and secondly the eruption has a distinctive character—it is widespread, and consists of guttate and nummular lesions resembling a secondary syphilide, for which it is not infrequently mistaken.

Swift [6] and other workers drew an analogy between some of the manifestations of tuberculosis, syphilis, and rheumatic fever, which may be pursued, and a comparison made between the latent period in the development of the secondary syphilide and the delay in the appearance of the psoriasis eruption following acute streptococcal infection, and between the rarity of the occurrence of neurosyphilis in patients who present a florid secondary rash, and the freedom of psoriasis patients from the graver complications of rheumatic infection.

I would submit that these three distinctive features of psoriasis in relation to rheumatic infections, namely (1) a latent period in the development of the eruption, (2) an initial distinctive type of eruption, and (3) immunity in after-life from such internal complications as valvular heart disease, point to the conclusion that there is some special relationship between psoriasis and rheumatic infection, and this conclusion is not invalidated by the fact that psoriasis may and does occur from a variety of other causes.

The frequency of the incidence of psoriasis in rheumatic cases is another aspect of the subject. The evidence obtained from hospitals for rheumatic diseases where the graver forms of rheumatic affections are assembled cannot be regarded as satisfactory or complete.

In conclusion I should like to point to some analogies in the various methods used in the treatment of psoriasis and of rheumatism.

For psoriasis, a low protein diet was at one time advocated [7] and used extensively, and in patients of the metabolic type who need a low protein intake, this diet is often beneficial, as in similar rheumatic cases. More recently it has been claimed [8] that the psoriasis patient is unable to assimilate fats, and success in the treatment of psoriasis by lowered fat diet has been reported. The most perfect fat-free diet is a raw fruit and raw vegetable diet, and the varied reports of the results of treatment of arthritis by this diet, and of psoriasis by a lowered fat diet are comparable. It is not, however, possible as yet to recognize the type of psoriasis patient who will respond. The treatment of psoriasis by physical methods has been largely confined to ultra-violet irradiation. Results vary. Generalized irradiation, with suberythematous doses is the most effective, and results obtained may probably be ascribed to the general tonic effect of this treatment. In regard to drug treatment, salicylates in psoriasis have no effect on cases with old chronic patches and chronic rheumatism, but are of value in the acute generalized cases. The local methods of treatment of psoriasis and of rheumatism seem on the surface to have little in common, but if one considers what has been termed *purely local treatment* of psoriasis [9], confinement to bed, baths, massage with a powerful counter-irritant (one authority recommends five to ten minutes daily friction), and immobilization by repeated applications of a coal-tar varnish, the analogy of methods becomes evident.

It affords a curious commentary on the subject under discussion that the lines of treatment, both internal and external, evolved from such widely divergent angles of thought, have converged so closely, for these conditions outwardly so dissimilar and unconnected, but having, in so many cases, common aetiological factors.

## REFERENCES

- 1 HUNT, E., *Lancet*, 1933 (ii), 351.
- 2 Id., *ibid.*
- 3 CLAWSON, B. J., *Ann. Int. Med.*, 1930-31, **4**, 433.
- 4 NAEGLI, O., DE QUEBVAIN, F., and STALDER, W., *Klin. Wochenschr.*, 1930, **9**, 924.
- 5 ZEIDLER, *Wien. med. Wochenschr.*, 1931, **81**, 877.
- 6 SWIFT, H. F., *Am. J. M. Sc.*, 1925, **170**, 691.
- 7 SCHAMBERG, J. A. M. A., 1932, **98**, 1633.
- 8 GRÜTZ and BÜROER, *Lancet*, 1934 (ii), 605.
- 9 *Lancet*, 1937 (ii), 1986.

**Dr. G. L. Kerr Pringle:** In discussing the association of skin manifestations in rheumatism and gout, I will divide the subject into two groups: (1) Anomalies of the skin in rheumatic disease. (2) Skin diseases in association with rheumatic disease.

*Group 1. Anomalies of the Skin in Rheumatoid Arthritis*

Most observers claim that there is a prodromal stage in rheumatoid arthritis in which the skin of the extremities is cold, the circulation is poor, and there is a tendency to chilblains. With the actual advent of the disease, profuse sweating of the palmar and plantar surfaces takes place, may extend to the dorsal aspect and may also affect the trunk. This is a characteristic cold sweat, and the palms and the flexor surfaces of the fingers are covered with an abundant dew. While the disease is active this cold sweating persists; as the acute attack passes off the sweating continues but loses its coldness. I am convinced that this is a useful clinical guide as to the progress of a case. In some cases it may persist for months and even years, while in others under treatment, or because of an intermission in the disease, the coldness, and later, the actual sweating, may disappear. Still later manifestations are atrophy of the skin, with pallor and glossiness, due to a vasoconstriction accompanying the arthritic complex. It is alleged by some writers that Raynaud's syndrome is to be regarded as the precursor of arthritis. It is quite certain that in some cases the syndromes of rheumatoid arthritis and Raynaud's disease run along parallel lines. Numbness, cyanosis of several fingers, pallor of others, with deep purple tips, accompanied with severe pain, passing on, with the severity of the disease, to a condition of absorption or necrosis of the terminal phalanges and nails. These are occasionally seen in rheumatoid arthritis. On the other hand Wardrop Griffith [1] has had under observation for a number of years cases of Raynaud's disease which have been accompanied by an arthritis very similar to that seen in rheumatoid arthritis.

*Pigmentary disturbance of the colour of the skin.*—Kent Spender [2] pointed out the frequency of concentrated patches of pigment occurring in cases of rheumatoid arthritis. The patches are of various sizes and may be found in many parts of the body. Across the forehead the pigment spreads as a light bronze smear, or like a dash of chloasma. Under the eyelids the streak of colour may be very dark and may shine with a metallic polish. The dominant tints on the face are lemon, orange, and citron. A bronze shadow can often be detected on the back of the hands; other unexposed parts of the body may be darkened in patches. In some cases the pigment may occur in spots which vary in size, a favourite site being the forearms. Patients will tell you that the "yellowness" and the spots began at the same time as the rheumatoid symptoms. These pigmented areas are, however, not confined to cases of rheumatoid arthritis, but are also seen in such conditions as molluscum fibrosum. For a number of years I have been on the look-out for cases of rheumatoid arthritis presenting pigmented areas, and I have come to the conclusion that the condition is not so common as Kent Spender claimed.

In osteo-arthritis we do not find cold sweating of the palms and soles, and the skin, instead of being smooth and glazed, is dry and rough, and approaches more to the state of skin found in hypothyroidism.

In the condition called Heberden's nodes—which is considered to be osteo-arthritis, but which may be a form of gout—the initial symptom consists of redness on the lateral aspect of the terminal joint of one or more of the digits. This redness is definitely localized and continues for a week or two, with some pain and subsequent swelling; the redness and pain disappear then, but the deformity remains. Later on, some other terminal joint may become affected and the same procedure take place.

In addition to the rheumatic nodules which are seen in acute rheumatism and sometimes in rheumatoid arthritis, one occasionally sees small rounded cyst-like bodies of the appearance of sago, on the knuckles in chronic rheumatoid arthritis. They may be mistaken for gouty tophi, but they contain clear fluid, are not painful, and appear gradually to become absorbed, leaving a fibrous thickening. I have no explanation to offer as to their nature.

#### *Group 2. Skin Diseases in Association with Rheumatic Diseases*

Patients constantly tell us that the chiropodists or manicurists say that their corns and callosities, or the state of their nails, are due to rheumatism. Is there any truth in this, or is it just a gratuitous statement on the part of the operators to show how well informed they are? I have always understood that corns and callosities were produced by pressure or by friction. That the pressure may be due to arthritic deformity of the small joints of the foot is quite possible, but the more probable causes are badly fitting shoes, thin silk and artificial silk stockings, and flat-foot. Nor can I believe that rheumatism, *per se*, can have any effect on the nutrition of the nails. Abnormalities of these appendages are much more likely to be due to gout, eczema, or trauma, as for instance, in too much manicuring.

John Freeman [3], discussing allergy and hypersensitivity, asks the questions: (1) Is rheumatism ever—or is it always—caused by infection? (2) If an infection is an essential causal factor of some, or of all, rheumatism, can the state produced thereby fairly or helpfully be called “allergy”?

“Concerning the infective cause of rheumatism, it is most significant to me that so many infections constituting well-marked clinical entities have rheumatic pains or rheumatic changes of structure as a prominent, or at least an occasional, feature. Thus we have Malta fever, gonorrhœa, typhoid, and the paratyphoids, indeed almost any of the coliform infections—dysentery, pneumonia, dengue, trench fever, influenza, and so forth, in fact it is harder to say which infections will not produce such symptoms than to say which will. If experts protest that these are not “true” rheumatism, select one of them—consider gonorrhœal arthritis: We have abundant evidence that infections can give rise to rheumatic symptoms, and that practically every infection can produce them on occasion. Rheumatism may be regarded as one of the possible sequelæ of invasion of the body by foreign organisms. So clearly is this the rule that I should be inclined to say that, if it could be proved that ‘rheumatic’ symptoms are in no way concerned with an infection, then they ought not to be called rheumatic, but some fresh name should be found for them.”

Many authorities, such as Pemberton [4], Osgood [5], and Hench [6] maintain that psoriasis, erythema, urticaria, &c., are frequently seen in cases of chronic rheumatic disease, especially psoriasis.

I had always accepted such views until eight years ago when I read at a meeting of the old Section of Balneology “A Summary of Two Thousand Consecutive Cases of Rheumatic Disease”<sup>1</sup>—1,200 hospital and 800 private cases, when my belief in such statements was shaken.

In this summary I found record of only 42 cases of skin disease mentioned :—

Psoriasis	...	...	...	17
Erythema and erythema nodosum	...	...	...	9
Eczema	...	...	...	9
Herpes zoster	...	...	...	1
Urticaria	...	...	...	5
Purpura	...	...	...	1

Again nothing was to be learned from the groups of rheumatic disease in which psoriasis was found :—

Subacute rheumatism	...	...	...	1
Fibrositis	...	...	...	4
Rheumatoid arthritis	...	...	...	6
Osteo-arthritis	...	...	...	3
Chronic villous arthritis	...	...	...	3

As I had not specially been looking for skin complications in these 2,000 cases, I asked Dr. Gasking, house physician at the Royal Bath Hospital, to take particular note of these. This he has very kindly done in 500 cases, with the following findings :—

Psoriasis	...	...	...	8
Dermatitis	...	...	...	4
Acne vulgaris	...	...	...	10
Erythema	...	...	...	2
Folliculitis	...	...	...	1 (20 cases)

If we deduct the cases of acne, we see that the percentage of psoriasis occurring in 2,500 cases is about 0·8%. This percentage of cases of psoriasis in arthritis does not agree with those of Dr. Elizabeth Hunt, and I would suggest that many of the cases were not rheumatic, but gout.

Dr. Barber has dealt with psoriasis arthropathica. In reading Garrod and Evans' [7] description of three cases, I particularly noticed that there was a definite history of hydro-arthrosis in two of the cases, and that all three cases started with a nervous shock. We know that a dormant psoriasis and also an eczema may become active following a nervous shock, and the same applies to many cases of rheumatoid arthritis.

The association of the erythema, erythema nodosum, erythema induratum (non-tuberculous), Bazin's disease, &c., i.e. infections with the tubercle bacillus streptococcus, gonococcus, &c., with pains in the limbs and joints, is called "rheumatic". So also are the symptoms produced by toxins circulating in the blood-stream from the ingestion of some red wines, strawberries, shellfish, &c., symptoms akin to those produced by the injection of sera. Surely we cannot include both in the same diagnostic pigeon-hole. The former we recognize as due to an infection; the latter may be due to errors of metabolism, or a hypersensitiveness. When due to an error of metabolism, the question of irregular gout at once arises; when due to a hypersensitiveness, then the question of allergy arises. Asthma and eczema are almost certainly produced by non-bacterial substances acting as allergic agents. Children often complain of pains in their limbs, occurring just before an attack of asthma.

The presence of eczema or, to use Cranston Low's term, "sensitization dermatitis", with rheumatic manifestations would appear to be accidental. In my summary of 2,000 cases there are only nine cases recorded. It is worthy of note that in this summary there were eight cases with a history of asthma recorded, six of these occurring in the rheumatoid group.

The allergic association of eczema and asthma, and its bearing on the possibility of allergy in chronic rheumatic disease, has not been proved. Some authorities speak of "streptococcal hypersensitivity" and claim that it may be a familial

predisposition, or shall I use the old-fashioned term *soil, hearth, or diathesis*? For instance, *erythema nodosum* is probably not a specific morbid entity, and may arise as easily in tuberculosis as in rheumatism, although in point of fact it may often be of streptococcal origin.

*Gout*.—I agree with Dr. Barber as to the influence of heredity and familial predisposition. I know of one family with a hereditary history of gout on both sides, with what was no doubt rheumatoid arthritis in the maternal grandmother, gout in the father, frequent attacks of severe urticaria in the mother, rheumatic fever, endocarditis and psoriasis in one daughter as a child, bone tuberculosis in another daughter, followed by enlarged cervical glands and fibrosis in later life, and gouty erythema in one son.

We are on much safer ground when we say that there is some association between certain skin affections and gout.

Gouty eczema occurs most frequently in the following situations: the external ear and around it, face and forehead, back of the neck, flexures of the joints, scrotum and prepuce, and round the anus, legs, and trunk. Dr. Barber has specially referred to erythema of the palmar and plantar surfaces, and also to hyperkeratosis. The nails of gouty subjects tend to become thin and brittle and usually present a longitudinal ridge producing the condition known as "reedy nail". *Herpes, pruritis, prurigo, and psoriasis*, are also seen in the gouty subject.

I am convinced that nowadays many cases of "irregular" or "abarticular gout" are missed. It is not necessary that there should have been acute attacks, but patients in whom some of the criteria of gout are present—e.g. heredity, presence of tophi, occasional attacks of arthritis, high blood urea, or Heberden's nodes—should make one consider whether one is not dealing with irregular gout rather than with rheumatic arthritis.

Many authorities consider that irregular gout has become more common. Prof. Cmunt of Prague [8] points out that in one series of cases the number of women affected more than equalled the number of males (32 females to 30 males). He explains this by the greater age, 77% being over 50, when the influence of the climacteric on the one hand, and commencing arteriosclerotic changes on the other, are not without significance. I have no statistics substantiating these views, but I suggest that this would be a good line of investigation to be carried out at the spa hospitals and rheumatic clinics. Many of these patients will tell you that they are better in general health when the skin condition is active.

Treatment should be particularly applied to the general condition, i.e. gout, rather than to the associated skin condition.

#### REFERENCES

- 1 GRIFFITH, WARDROP, *Med. Chronicle*, Nov. 1891, Oct. 1902.
- 2 SPENDER, KENT, "Allbut's system of medicine", **3**, 88.
- 3 FREEMAN, JOHN, "Allergy and hypersensitiveness", R. C. P. "Report on chronic rheumatic diseases", **1**, 40.
- 4 PEMBERTON, R., "Arthritis and rheumatoid conditions", 1929.
- 5 PEMBERTON and OSGOOD, "Management of chronic arthritis", 1934, 149.
- 6 HENCH, "Acute and chronic arthritis", Nelson Loose-leaf Surgery, 1935.
- 7 GARROD and EVANS, *Quart. J. Med.*, 1924, **17**, 171.
- 8 CMUNT, Prof. E., *Arch. M. Hydrol.*, 1936, **14**, 146.

**Dr. W. Yeoman**: I propose to confine my remarks to the treatment of these cases from the spa point of view and particularly that of the Harrogate Spa. At the outset I should say that since the advent of light and X-ray treatment there has been a marked diminution in the number of skin cases coming to the spas.

Since the Great War there have been fewer cases of old-fashioned gout, and in consequence we have seen less of the generalized gouty eczema which so frequently accompanies or alternates with an acute attack of gout. Dr. Barber has mentioned

the more local skin lesions which appear in gouty subjects with a high blood-uric-acid content and Dr. Kerr Pringle has emphasized his opinion as to the prevalence of irregular gout, an opinion with which I unhesitatingly agree.

It is interesting to note that shortly after the War and during the depression, gout became a rare disease and for some years we hardly saw a case at the Harrogate Royal Bath Hospital. I was particularly struck by this, as I was privileged to visit the Mineral Water Hospital at Bath about that time and saw a number of cases of gout, which, I thought, might be due to the consumption of cider in that area, cider being a cheaper drink than beer. Since the general increase in the consumption of beer we are now seeing more cases of gout in Harrogate.

In recent years the Harrogate sulphur waters have been the subject of experimental work. Brown and Woodmansey, as a result of exhaustive work which was reported at a meeting of the Section of Balneology in January 1929,<sup>2</sup> found that the old sulphur water caused a rise of 6% in the excretion of total nitrogen, an increase of 10% in the excretion of creatinine, and an increase of 10% in the excretion of endogenous urea. The early work of Bain on the cholagogic effects of the water has been confirmed by some unpublished work of his son, Dr. Curtis Bain. By means of the duodenal tube he was able to demonstrate the free secretion of A and B bile in normal people within two minutes of passing 10 c.c. of sulphur water down the tube. We hope in the near future to investigate by these methods what effect the sulphur water has in the rheumatic and gouty patient, particularly those with achlorhydria.

As far as Harrogate is concerned I consider that the beneficial effect of the waters in these cases is first of all produced by the stimulating action on the liver, and secondly by the immersion in the waters. In the case of acute gouty eczema it is impossible to give sulphur baths, but after a week or so of drinking the waters it is usually possible to start cautiously with an alkaline sulphur bath which, as improvement sets in, can be given daily.

The work of Woodmansey and Lissimore has shown that, *in vitro*, the sulphur group of waters are strongly bactericidal, and by means of the intestinal douche, as given at Harrogate, are enabled to exercise their maximum effect on the mucosa of the large intestine. This I consider to be a valuable method to use at the commencement of the cure of the cases showing a skin lesion, for to my mind these lesions are partly due to the excretion through the skin of a metabolic irritant.

Turning now to the cases of psoriasis. The association of rheumatism with psoriasis may be a coincidence, but when they occur in the same subject there seems to be a common factor in their causation. As Dr. Barber has mentioned, one frequently sees the rheumatism diminish and the psoriasis increase, and vice versa. It is significant that it is usually the infective rather than the degenerative type of arthritis which is present in these cases. Owing to the nature of psoriasis to wax and wane it is difficult to assess the value of any treatment, but I feel that this condition is eminently suitable for treatment at a spa. The waters, taken internally, alter metabolism and expedite excretion, as I have endeavoured to show, and bathing in the water has a macerating action on the scales and enables the action of chrysarobin or other agent to be more rapidly effective. In my experience psoriasis treated on these lines does not relapse so quickly.

In conclusion, I would stress my opinion that spa treatment acts by altering the metabolism of the patient and is thus most suitable for treating skin lesions which are associated with an alteration in metabolism, particularly those dealt with in this discussion.

<sup>2</sup> *Proceedings*, 1929, 22, 488 (Sect. Balneo. and Climat., 1).





# In Convalescence after Influenza, Pleurisy, Pneumonia, Bronchitis

The soothing, inflammation-allaying properties of 'Angiers' and its general tonic effect especially commend its use in convalescence from acute respiratory affections. It will clear up any remaining catarrh, whether of the respiratory or digestive organs. It will restore tone to the digestive functions, and greatly improve assimilation and nutrition.

An absolutely perfect emulsion, it is presented in a form pleasing to the taste, and acceptable to the most fastidious. Moreover, it can be administered to advantage in conjunction with other remedies, such as salol, aspirin, bismuth, etc.

'Angiers' is made with petroleum specially purified for internal use. It is the original petroleum emulsion, the result of many years of careful research and experiment.

*Free Samples to the Medical Profession*

THE ANGIER CHEMICAL COMPANY, LIMITED  
(Dept. B.92), 86, CLERKENWELL ROAD, LONDON, E.C.1



# ACRIFLAVINE —BOOTS—

**A**CRIFLAVINE — BOOTS is one of the safest and most potent of modern antiseptics ; indicated in the treatment of all local septic conditions.

Supplied as follows :—

Powder, Solution Tablets, Medicated Gauze, Cream, Pessaries, Bougies and as an Emulsion.

BISMOSTAB                    THIOSTAB  
SULPHOSTAB                STABILARSAN  
are Boots Products and  
are obtainable through all branches of



WHOLESALE AND EXPORT DEPARTMENT  
**BOOTS PURE DRUG CO. LTD**  
NOTTINGHAM - - - ENGLAND

TELEPHONE:  
NOTTINGHAM 45501

TELEGRAMS:  
DRUG NOTTINGHAM

